UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

TAKEDA PHARMACEUTICAL CO., LTD., ET AL.,

Plaintiffs,

v.

HANDA PHARMACEUTICALS, LLC,

Defendant.
_____/

RELATED CASES

TAKEDA PHARMACEUTICAL CO., LTD., ET AL.,

Plaintiffs,

v.

ANCHEN PHARMACEUTICALS, INC., AND TWI PHARMACEUTICALS, INC.,

Defendants.
_____/

TAKEDA PHARMACEUTICAL CO., LTD., ET AL.,

Plaintiffs,

v.

IMPAX LABORATORIES, INC.,

Defendant.
_____/

Case No. C-11-00840 JCS

Related Case Nos. C-11-1609 JCS and C-11-1610 JCS

CLAIM CONSTRUCTION ORDER

I. INTRODUCTION

Takeda Pharmaceutical Co., Ltd., Takeda Pharmaceuticals North America, Inc., Takeda Pharmaceuticals LLC, and Takeda Pharmaceuticals America, Inc. (hereinafter, referred to collectively as "Takeda") initiated these three related patent infringement actions ("the Actions") under 35 U.S.C. § 271(e)(2), a provision of the Hatch-Waxman Act, in response to Abbreviated New Drug Applications ("ANDA") submitted to the U.S. Food and Drug Administration ("FDA") by Handa Pharmaceuticals, Inc. ("Handa"), Anchen Pharmaceuticals, Inc. ("Anchen"), TWi Pharmaceuticals, Inc. ("TWi"), and Impax Laboratories, Inc. ("Impax").[1] In their ANDAs, Defendants seek FDA approval to manufacture and sell generic versions of Takeda's drug DEXILANT (dexlansoprazole), a prescription drug used to treat acid reflux disease. Takeda owns several patents related to dexlansoprazole.

The following Takeda patents are at issue in the Actions: 1) U.S. Patent No. 6,462,058 ("the '058 Patent"); 2) U.S. Patent No. 6,664,276 ("the '276 Patent"); 3) U.S. Patent No. 6,939,971 ("the '971 Patent"); 4) U.S. Patent No. 7,737,282 ("the '282 Patent"); 5) U.S. Patent No. 7,285,668 ("the '668 Patent") and 6) U.S. Patent No. 7,790,755 ("the '755 Patent").

The parties conducted a tutorial on February 2, 2012. A claim construction hearing was held on February 16, 2012. The Court's final constructions are set forth below.[2]

II. BACKGROUND RELATING TO THE CLAIMED TECHNOLOGY

A. Crystals

Crystals are solids in which the atoms (or molecules) are arranged in a periodic repeating pattern that extends in three dimensions. Declaration of Allan S. Myerson, Ph.D., in Support of Takeda's Opening Claim Construction Brief ("Myerson Decl.") ¶ 21; Declaration of Wayne J. Genck, Ph.D. ("Genck Decl.") ¶ 16. The smallest repeating unit in a crystal is the "unit

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[1] Anchen and TWi are codefendants in Case No. C-11-01609 JCS. Hereinafter, the Court refers to them collectively as "TWi."

[2] The parties have consented to the jurisdiction of the undersigned United States Magistrate Judge pursuant to 28 U.S.C. § 636(c).

cell," which is "essentially a box with a specific size and shape that contains a particular number of atoms and molecules in a well-defined arrangement." Genck Decl. ¶ 22. The unit cell, as well as the arrangement of atoms and molecules within it, is the defining characteristic of a given crystalline form. *Id*. The unit cells are packed together in the crystal in a lattice structure, which is made up of a repeating pattern of individual unit cells. *Id*. ¶ 23. The lattice can be characterized in terms of three spatial dimensions – a, b, and c – and three angles – alpha, beta and gamma. Myerson Decl. ¶ 26. These lengths and angles are known as "lattice parameters." *Id*. The shape of the unit cell, including the axes that form the borders of the unit cell and the angles between those axes, defines a series of "lattice planes" in the crystal. Genck Decl. ¶ 29 (citing Myerson Decl., Ex. 19 (Bhattacharya Article) at DEX0014478).

B. X-ray Crystallography

X-ray diffraction is a technique used to identify crystals and to determine crystal structure. Myerson Decl. ¶ 28; Genck Decl. ¶ 25. Crystal structure can be analyzed using single crystal x-ray diffraction or x-ray powder diffraction ("XRPD"). Myerson Decl. ¶ 29; Genck Decl. ¶ 25. In XRPD, crystalline material is ground into a fine power and irradiated with x-rays of a certain wavelength (referred to as "λ"), at a range of different angles (referred to as "2θ" or "two-theta" angles). Genck Decl. ¶ 28 (citing Myerson Decl., Ex. 12 (Myerson Article) at DEX0014616). A diffractometer measures the intensity of the X-rays that diffract from the sample across a range of diffraction angles. Myerson Decl. ¶ 31; Genck Decl. ¶ 32. The instrument then produces a plot of the two-theta values versus the intensity of the diffracted x-rays, called a "diffractogram." Myerson Decl. ¶ 31; Genck Decl. ¶ 28. For a crystalline material, the diffractogram has a number of peaks of various heights, with each peak appearing at a particular two-theta angle value. Genck Decl. ¶ 28. This pattern of peaks acts as a signature or fingerprint for the substance. Myerson Decl. ¶ 32; Genck Decl. ¶ 32.

When X-rays of a particular wavelength reflect off parallel planes in the crystal, the diffractometer registers an increase in intensity when the reflected X-rays are "in phase" with each other, which occurs only when two parallel planes are separated by a particular distance, referred to

as "d." Myerson Decl. ¶30; Genck Decl. ¶ 30. The distances "d", or "d-spacings," are mathematically related to both the wavelength (λ) and angle (two-theta) of the incoming X-rays according to an equation known as Bragg's Law. Myerson Decl. ¶30; Genck Decl. ¶ 31. Under Bragg's Law, $n\lambda = 2d \sin \theta$, where n is an integer (usually 1), λ is the wavelength, d is the d-spacing, and θ (theta) is the angle of incidence of the X-rays relative to the crystal. Myerson Decl. ¶ 30; Genck Decl. ¶ 31.

C. Enantiomers

Enantiomers are pairs of compounds that contain chemical formulas and atomic sequences that are identical to one another except that they are non-superimposable mirror images of one another, just as a person's left and right hands are non-superimposable images of each other. Meyerson Decl. ¶ 39; Genck Decl. ¶ 42. Enantiomers, which also are known as chiral molecules, are designated as right (R+) and left (S-), or (+) and (-). Myerson Decl. ¶ 39. The patents-in-suit relate to dexlansoprazole, which is an enantiomer of lansoprazole.. Genck Decl. ¶ 77.

D. Thermal Analysis

One way to characterize crystals is through the use of "thermal analysis," which explores the way a sample behaves over a range of temperatures. Genck Decl. ¶ 33. Thermal analysis can be used to analyze a crystal sample for various phase transitions, that is, transitions between states of matter, such as solid phase to liquid phase or liquid phase to gas phase. *Id*. ¶¶ 33-34. A parameter that is often used to characterize a crystal form using thermal analysis is the crystal's melting properties. *Id*. ¶ 35. The melting properties of a particular sample of a crystalline material are directly related to the purity of the sample. *Id*. In particular, a pure crystal form melts at a well-defined, characteristic temperature whereas a sample that includes impurities generally melts over a broader temperature range. *Id*.

A variety of methods can be used to analyze a crystal's melting properties. *Id*. One such method is differential scanning calorimetry ("DSC"). *Id*. ¶ 37; Myerson Decl. ¶ 41. DSC is a technique in which the difference in the amount of heat required to increase the temperature of a sample and a reference is measured as a function of temperature. Myerson Decl. ¶ 41. The DSC instrument creates a plot of the amount of energy required to maintain the sample crystal at a given

temperature over the time of the experiment. Genck Decl. ¶ 39. At or near a crystal's melting point, there is a peak in the DSC curve. Myerson Decl. ¶ 43. In the case of a pure crystalline solid, the peak will be sharp, corresponding to melting only at or near its melting point. Genck Decl. ¶ 40. On the other hand, where impurities are present, the DSC curve is more gradual because heat flow may be detected before the actual melting of the sample, resulting in a gradual departure of the curve from the baseline. Genck Decl. ¶ 40.

Other techniques for assessing the melting point of a crystal are the capillary method and hot stage microscopy. Genck Decl. ¶¶ 36, 41. The capillary method uses a capillary tube containing a small amount of the test compound, which is immersed in an oil bath that is heated slowly. *Id*. ¶ 36. The transition from solid to liquid is observed visually through a magnifier on the instrument, or is detected optically by the instrument itself. *Id*. Hot stage microscopy involves slowly heating a solid sample on the viewing stage of a microscope across a range of temperatures and visualizing the sample transitions as a function of temperature. *Id*. ¶ 41.

E. The Patents-in-Suit

The patents-in-suit relate to compositions of, or methods of treatment using, dexlansoprazole, a drug classified as a proton pump inhibitor ("PPI") that is used to treat acid reflux and gastroesophageal reflux disease ("GERD") by reducing the amount of gastric acid produced in the stomach. *See* Myerson Decl. ¶ 44; Declaration of George Triadafilopoulos ("Triadafilopoulos Decl.") ¶ 23. The asserted claims from the '058, '276, '668 and '971 patents relate to crystal forms of dexlansoprazole, while the '282 patent relates to an amorphous (that is, non-crystalline) compound of dexlansoprazole. The '755 patent relates to controlled-release compositions for imidazoles, a class of compounds of which dexlansoprazole is a member. The asserted claims of the '755 patent are specifically directed at a composition that uses a dual-delayed release mechanism with two different types of enteric coatings.

The '668 patent claims dexlansoprazole crystals different from, and developed later than, those claimed in the '058 and '971 patents. In the specification of the '668 patent, the inventors explain that the relatively high "melting start temperature" of the crystal form of dexlansoprazole disclosed in the '668 patent distinguishes it from the dexlansoprazole crystal forms disclosed in

the earlier patents. '668 patent, col.12, ll. 35-41. According to the inventors, because of this higher melting start temperature, the disclosed crystal form has "superior preservation stability and can be used advantageously as a pharmaceutical product" as compared to the crystal forms in the prior art with lower melting start temperatures. *Id*.

III. LEGAL STANDARDS

A. Claim Construction Standards

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). Generally, claim terms are given the ordinary and customary meaning that would be ascribed to them by a person of ordinary skill in the field of the invention. *Id*. at 1312-1313; *see also Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1342 (Fed. Cir. 2001)("[U]nless compelled to do otherwise, a court will give a claim term the full range of its ordinary meaning as understood by an artisan of ordinary skill").

The most "significant source of the legally operative meaning of disputed claim language" is the intrinsic evidence of record, that is, the claims, the specification and the prosecution history. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). This is because "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313. In some cases, the specification may reveal a "special definition" given by the inventor that differs from the meaning the term might otherwise possess. *Id*. at 1316. In such instances, "the inventor's lexicography governs." *Id*. Similarly, a specification may reveal "an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id*.

A person of ordinary skill in the art also looks to the prosecution history of a patent to understand how the patent applicant and the Patent Office understood the claim terms. *Id*. at 1313, 1317. Arguments and amendments made during patent prosecution limit the interpretation of claim terms to exclude interpretations that were disclaimed to obtain allowance of a claim. *Southwall Technologies, Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995).

While claims are to be construed in light of the specification, courts must be careful not to read limitations from the specification into the claim. *Phillips*, 415 F.3d at 1323. Thus, for example, if a patent specification describes only a single embodiment of a claimed invention, that does not mean the claims of the patent necessarily must be construed as limited to that embodiment. *Id*. Rather, it is understood that the purpose of the specification "is to teach and enable those of skill in the art to make and use the invention" and that sometimes, the best way to do that is to provide an example. *Id*.

Courts may also use extrinsic evidence in construing claim terms if it is necessary, so long as such evidence is not used to "vary or contradict the terms of the claims." *Markman v Westview Instruments, Inc.,* 52 F.3d 967, 981 (Fed. Cir. 1995). As the court explained in *Markman*, "[extrinsic] evidence may be helpful to explain scientific principles, the meaning of technical terms, and terms of art that appear in the patent and prosecution history." 52 F.3d at 980. The Federal Circuit has warned, however, that such evidence is generally "less reliable than the patent and its prosecution history in determining how to read claim terms." *Phillips*, 415 F.3d at 1318. Thus, courts are free to consult dictionaries and technical treatises so long as they are careful not to elevate them "to such prominence . . that it focuses the inquiry on the abstract meaning of the words rather than on the meaning of claim terms within the context of the patent." *Id*. at 1321-22.

B. Indefiniteness Standards

The requirement that claims be sufficiently "definite" is set forth in 35 U.S.C. § 112, ¶ 2, which provides that, "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." "The definiteness inquiry focuses on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the rest of the specification." *Union Pacific Resources Co. v. Chesapeake Energy Corp.*, 236 F.3d 684, 692 (Fed. Cir. 2001). In order to "accord respect to the statutory presumption of patent validity," a claim should be found indefinite "only if reasonable efforts at claim construction prove futile." *Exxon Research and Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001). A claim is not indefinite simply because its meaning is not ascertainable from the face of the claims. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d

1311, 1342 (Fed. Cir. 2003). Nor is a claim indefinite simply because it covers "some embodiments that may be inoperable." *Exxon Research and Engineering Co.*, 265 F.3d at 1382. A claim is indefinite, however, if it is "insolubly ambiguous, and no narrowing construction can properly be adopted." *Amgen*, 314 F.3d at 1342 (citations omitted). To establish that a claim is indefinite an alleged infringer must "demonstrate by clear and convincing evidence that one of ordinary skill in the relevant art could not discern the boundaries of the claim based on the claim language, the specification, the prosecution history, and the knowledge in the relevant art." *Haemonetics Corp. v. Baxter Healthcare Corp.*, 607 F.3d 776, 783 (Fed. Cir. 2010).

IV. CONSTRUCTION OF CLAIM TERMS

The parties submitted ten claim terms for construction, consistent with Patent Local Rule 4-3 and the Court's Case Management and Pretrial Order [Docket No. 51]. The Court addresses these claim terms below.

A. "a crystal of" ('058 patent, claims 1-4/ '668 patent, claims 9-10), "a crystalline compound of" ('276 patent, claims 2 and 3/ '971 patent, claims 6-8)

1. Contentions of the Parties

Proposed Construction of Takeda, Impax and Handa	Proposed Construction of TWi
regularly repeating pattern of molecules with long range order extending in three dimensions	plain meaning

Claims 2 and 3 of the '276 patent and claims 6-8 of the '971 patent are directed to a "crystalline compound" of dexlansoprazole; claims 1-4 of the '058 patent and claims 9 and 10 of the '668 patent are directed to a "crystal of" dexlansoprazole. The parties agree that these claim terms are used interchangeably and therefore may be considered together. Takeda, Impax and Handa have proposed a construction of these claim terms based on what they assert is their plain and ordinary meaning, while TWi contends that the terms do not require construction.

According to Takeda, Impax and Handa, the proposed construction of these claim terms is consistent with the plain and ordinary meaning of the terms as they have long been understood by

those skilled in the art.[3] Takeda notes that the definition for a crystal set forth in the extrinsic evidence offered by TWi in connection with its claim construction position is consistent with the construction offered by Takeda, Impax and Handa. *See* Myerson Decl. ¶ 58 & Ex. 15 at 510 (IPXL - 0009909) (*McGraw-Hill Concise Encyclopedia of Science and Technology*, Sybil P. Parker ed., 3d ed. 1994 (defining a "crystal" as a "solid throughout [in] which the atoms and molecules are arranged in a regularly repeating pattern")).

Takeda further contends that it will be helpful to the Court to construe these claim terms to "elucidate[ ] the structural characteristics that define a crystal" and to "clarify the link between the 'crystal' claim requirement and the empirical determination of whether the accused products contain crystals, as the regularly repeating three-dimensional molecular order that characterizes a crystalline solid can be confirmed or refuted through methods such as the x-ray powder diffraction analysis technique referred to in several of the claims." Takeda's Opening Claim Construction Brief at 10.

TWi does not dispute that the proposed definition of "crystal" and "crystalline compound" offered by Takeda, Impax and Handa "recites a 'characteristic' of a crystal." Defendants' Claim Construction Brief at 7 (citing Declaration of Parisa Jorjani in Support of Defendants' Claim Construction Brief ("Jorjani Decl."), Ex. 1 (Myerson Dep.) at 215-216). It argues, however, that the

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[3]Takeda cites to the following extrinsic evidence in support of its proposed construction of these claim terms: Myerson Decl. ¶ 56 ("It is my opinion . . . that a person of ordinary skill in the art, reading the crystal-form patents in 1999, would have understood the disputed term "a crystal of" and "a crystalline compound of" to be "a regularly repeating pattern of molecules with long range order extending in three dimensions"), ¶57 (citing the following "literature references that are accepted authorities in the field of crystallography" in support of proposed construction: Ex. 9, at DEX0014501 (C.W. Bunn, Chemical Crystallography (2d ed. 1961)) ("crystalline" means that "the atoms or molecules of which [a solid substance is] composed are packed together in a regular manner, forming a three-dimensional pattern"); Ex. 10, at DEX0014581 (Bruno C. Hancock and George Zografi, Characteristics and Significance of the Amorphous State in Pharmaceutical Systems, 86 J. Pharm. Sci. 1-12, 1 (1986) (hereinafter, "Hancock and Zografi")) ("crystalline material" normally possesses "three-dimensional long-range order"); Ex. 11, at DEX0014512 (S.R. Elliott, Physics of Amorphous Materials 1-6 (2d ed. 1990)) ("A perfect crystal is that in which the atoms (or groups of atoms or 'motifs') are arranged in a pattern that repeats periodically in three dimensions to an infinite extent"); Ex. 12, at DEX0014612 (Allan S. Myerson and Rajiv Ginde, Crystals, Crystal Growth, and Nucleation, in Handbook of Industrial Crystallization 33 (2d ed. 2002)) ("Crystals are solids in which the atoms are arranged in a periodic repeating pattern that extends in three dimensions"); Ex. 13, at DEX0014770 (Richard Zallen, The Physics of Amorphous Solids 1-5 (2004)) (stating that, "in crystals, "[t]he atomic positions exhibit long-range order"); Ex. 14, at DEX0014719 (Hsien-Hsin Tung et al., Crystallization of Organic Compounds: An Industrial Perspective 25 (2009)) ("crystalline materials are solids in which molecules are arranged in a periodical three-dimensional pattern")).

Court should not construe these terms because they are well understood and have an established meaning. *Id*. According to TWi, construction of these claim terms not only is not required but also "makes no sense in many respects and creates ambiguity where none previously existed." *Id*. In particular, TWi asserts that "if one substitutes the proposed definition for the word 'crystal' as it appears in the patent specification, it would not be consistent with how the term was actually used throughout the specification." *Id*. In support of this contention, TWi cites deposition testimony of Takeda's expert, Dr. Myerson, offered in connection with the '058 and '668 patents. *Id*. (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 197, 214).

First, as to the '058 patent, TWi cites Dr. Myerson's testimony that if the phrase "a crystal" were replaced with Takeda's proposed definition of this term in Example 1 of the '058 patent (described in column 10), the resulting statement is "very wordy." *See* Jorjani Decl., Ex. 1 (Myerson Dep.) at 214. Second, as to the '668 patent, TWi cites Dr. Myerson's opinion that in connection with claim 9 of the '668 patent, directed to "a crystal" of dexlansoprazole having a melting start temperature of not lower than 131 degrees Celsius, multiple crystals of dexlansoprazole would be required to determine the melting start temperature using the DSC method because "you normally would not find a single crystal to do a DSC on." *Id*. at 197. Therefore, in that context "a crystal" of dexlansoprazole meant "crystalline dexlansoprazole," according to Dr. Myerson. *Id*.

Finally, TWi contends that if the Court were to adopt the construction proposed by Takeda, Impax and Handa, there would likely be a "new round of disputes regarding the meaning of the words used in the construction, such as 'regularly,' 'repeating,' and 'long-range order.'" Defendants' Claim Construction Brief at 8.

In its Reply Claim Construction Brief, Takeda dismisses TWi's assertion that the proposed construction will create ambiguity, arguing that TWi has failed to identify any such ambiguity. Takeda's Reply Claim Construction Brief at 1. According to Takeda, the proposed construction of these terms is "similar to that adopted by other courts." *Id*. (citing *Pfizer Inc. v. Dr. Reddy's Laboratories Ltd*., 2011 WL 767849, at *1 n.2 (D. Del. Feb. 28, 2011) (construing "crystalline" as "a solid form having a long range periodic ordered structure extending in three dimensions").

2. Analysis

"[T]he Federal Circuit has held that if commonly understood words are used, then the 'ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words.'" *Board of Trustees of Leland Stanford Junior University v. Roche Molecular Systems, Inc.*, 528 F. Supp. 2d 967, 976 (N.D. Cal. 2007) (quoting *Phillips*, 415 F.3d at 1314). Thus, in *Board of Trustees of Leland Stanford Junior University*, the Court held that the claim terms "therapeutically effective" and "therapeutically ineffective" required no construction because "they are neither unfamiliar to the jury, confusing to the jury, nor affected by the specification or prosecution history." *Id*. (citing *United States Surgical Corp. v. Ethicon, Inc*., 103 F.3d 1554, 1568 (Fed.Cir.1997)).

On the other hand, even if a claim term has a plain and ordinary meaning, the court should construe the term if construction is required to resolve a dispute about the scope of the asserted claims, which is a question of law to be decided by the Court. *O2 Micro Intern. Ltd. v. Beyond Innovation Technology Co., Ltd.*, 521 F.3d 1351, 1361 (Fed. Cir. 2008). In *O2*, for example, the Federal Circuit held that the district court had erred in declining to construe the claim term "only if," because although the phrase had a "common meaning," the parties disagreed as to its scope. *Id*. at 1362. In other words, the court explained, the district court "failed to resolve the parties' dispute because the parties disputed not the meaning of the words themselves, but the scope that should be encompassed by this claim language." *Id*. at 1362.

Here, the parties seeking construction of these claim terms have identified no dispute or ambiguity that requires that the Court construe the terms. Nonetheless, the Court finds that construction of the term "a crystal" and "crystalline compound" is appropriate because these terms, unlike the claim terms at issue in cases where courts have found that no construction is necessary, such as *Board of Trustees of Leland Stanford Junior University*, are not so familiar that their meaning would be readily understood by a jury (or the Court) without construction.

Having found that construction of these claim terms is appropriate, the Court next addresses

whether the construction proposed by Takeda, Impax and Handa should be adopted in light of the concerns expressed by TWi. The Court concludes that it should.

First, while TWi contends that the proposed construction will simply result in a "new round" of disputes arising out ambiguities in the proposed construction, no actual dispute has been identified in this respect. Therefore, the Court rejects this argument.

Second, the Court finds unpersuasive TWi's assertion that "if one substitutes the proposed definition for the word 'crystal' as it appears in the patent specification, it would not be consistent with how the term was actually used throughout the specification." In support of this position, TWi relies on the testimony of Dr. Myerson that substitution of the word "a crystal" with the words of the proposed construction would make an example in the '058 patent specification "very wordy." Dr. Myerson went on to say, however, that the description would mean the same thing either way. *See* Jorjani Decl., Ex. 1 (Myerson Dep.) at 214.

The Court also rejects TWi's suggestion that the proposed construction of these claim terms may be inadequate because it merely describes "a characteristic" of "a crystal" or a "crystalline compound" rather than defining those terms. Again, TWi relies on Dr. Myerson's deposition testimony in support of its position. Dr. Myerson's testimony, however, supports the opposite conclusion. In particular, the following exchange occurred at Dr. Myerson's deposition:

Q: Well, lets turn to your definition of "amorphous compound." You say that an amorphous compound as used in the '282 patent, it means "a noncrystalline solid that lacks the long-range order characteristic of a crystal."

A: That's correct.

Q: So isn't it fair to say that this long-range order that you're talking about is a characteristic of a crystal?

. . .

A: It's the definition of a crystal. If you don't have the long-range order, it's not a crystal.

Q: . . .then why did you choose the word "characteristic" when you . . . offered a definition for "amorphous compound," why did you call the long-range order a "characteristic of a crystal"?

. . .

A: Well, it is a characteristic of a crystal because it is the definition of a crystal.

Jorjani Decl., Ex. 1 (Myerson Dep.) at 215-216. Therefore, the Court rejects TWi's contention that the proposed construction falls short because it merely describes "a characteristic"of "a crystal" or "crystalline compound."

For the reasons stated above, the Court adopts the construction proposed by Takeda, Impax and Handa for the claim terms "a crystal" and "crystalline compound."

B. "characteristic peaks at interplanar spacings (d)" ('058 patent, claims 1 and 2/ '971 patent, claims 7 and 8)

1. Contentions of the Parties

Takeda's Proposed Construction	Defendants' Proposed Construction
Peaks in the X-ray powder diffractogram of a crystal that uniquely identify that crystal, denoted by distances between lattice planes in a crystal as measured by a diffraction experiment and defined by Bragg's law, within normal experimental error of X-ray powder diffraction[4]	Peaks in the X-ray powder diffractogram of a crystal that uniquely identify that crystal, denoted by distances between lattice planes in a crystal as measured by a diffraction experiment and defined by Bragg's law

The term "characteristic peaks at interplanar spacings (d)" appears in claims 1 and 2 of the '058 patent and in claims 7 and 8 of the '971 patent. In each of these claims, the recitation of this term is followed by a list of eleven numbers, corresponding to the d-spacings of the particular crystal forms.

The parties agree that this claim limitation refers to measurements obtained through the x-ray powder diffraction method. *See* Myerson Decl. ¶ 62. The only dispute between Takeda and Defendants is whether or not the term should be construed so as to incorporate the experimental

[4]In Takeda's Opening Claim Construction Brief, it proposed that the term be construed as "a series of peaks that are characteristic of a particular crystal form within normal experimental error of x-ray powder diffraction." Takeda's Opening Claim Construction Brief at 8. In its reply brief, however, Takeda agreed to Defendants' more specific proposed construction, so long as the Court also included in its construction the phrase "within normal experimental error of X-ray powder diffraction." Takeda Reply Brief on Claim Construction at 2.

error that is associated with the measurement of the diffraction peaks and corresponding d-spacings.

In its Opening Claim Construction Brief, Takeda argues that at the time of the inventions of the '058 and '971 patents, both of which have a priority date of June 17, 1999, it was "universally recognized . . . that x-ray powder diffraction techniques involve some degree of experimental error." Opening Claim Construction Brief at 11 (citing Myerson Decl. ¶ 63) (stating that "[a] person of ordinary skill in 1999 would have understood any description of 'characteristic peaks of interplanar spacings (d)' to be within the context of the normal experimental error inherent to XRPD measurements because of limitations in the measuring equipment or techniques"). In support of this contention, Takeda points to the United States Pharmacopeia ("USP"), which establishes standards for medicines that are used by regulatory agencies and manufacturers. *Id*. The 1995 edition of the USP states that when using XRPD to compare a known material (the "reference") with an unknown material (the "sample"):

> [a]greement between sample and reference should be within the calibrated precision of the diffractometer for diffraction angle (2θ values should typically be reproducible to ±0.10 or 0.20 degrees), while relative intensities between sample and reference may vary up to 20 percent.

Id. (citing Myerson Decl., Ex. 16 at DEX0014738 ("X-Ray Diffraction," The United States Pharmacopeia, 1844 (23rd rev. 1995)). Takeda notes that the 2002 edition of the USP provided for the same range of error as to the diffraction angle values as the 1995 edition, while the 2005 USP narrowed the range of error to ±0.10 degrees (rather than ±0.10 or 0.20 degrees) for those values, reflecting improvements in XRPD technology. *Id*. (citing Myerson Decl., Ex. 17 (2002 USP excerpt), Ex. 18 (2005 USP excerpt)).[5]

Takeda also points to other references that its asserts reflect the understanding of a person skilled in the art that the measurement of the peaks of interplanar spacings (d) allowed for a range of

[5]The later versions of the USP do not set forth a specific range of error as to relative intensities, instead acknowledging that they may "vary considerably." *Id*.

error. First, Takeda cites to Sisir Bhattacharya et al., Thermoanalytical and Crystallographic Methods, in Polymorphism in Pharmaceutical Solids, 318-46 (2d ed. 2009), which states as follows:

> The United States Pharmacopeia contains a general chapter on XRD . . . , which sets the criterion that identity is established if the scattering angles in the powder patterns of the sample and reference standard agree to within the calibrated precision of the diffractometer. It is noted that it is generally sufficient that the scattering angles of the ten strongest reflections obtained for an analyte agree to within either ±0.10 or 0.20° 2θ, whichever is more appropriate for the diffractometer used. Older versions of the general test contained an additional criterion for relative intensities of the scattering peaks, but it has been noted that relative intensities may vary considerably from that of the reference standard, making it impossible to enforce a criterion based on the relative intensities of corresponding scattering peaks.

Id. at 11-12 (citing Myerson Decl., Ex. 19, at DEX0014482).

Second, Takeda cites to Harry G. Brittain, "Methods for the Characterization of Polymorphs and Solvates," in Polymorphism in Pharmaceutical Solids, 227, 236 (1st ed. 1999) – a reference that was cited by Defendants in the Joint Claim Construction and Prehearing Statement – in which the author quotes with approval the USP standard. *Id*. at 12 (citing Myerson Decl., Ex. 20 at IPXL - 0009873). In particular, Brittain states that the "USP general chapter on x-ray diffraction states that identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within ±0.20 degrees with that of the reference material, and if the relative intensities of these reflections do not vary by more than 20 percent." *Id*.

Defendants respond that Takeda's proposed construction improperly imports the notion of "experimental error" from extrinsic evidence. Defendants' Claim Construction Brief at 9 (citing *Callicrate v. Wadsworth Mfg., Inc.*, 427 F.3d 1361, 1368 (Fed. Cir. 2005)). The intrinsic evidence, Defendants contend, does not support Takeda's proposed construction. *Id*. Defendants point out that Takeda's expert, Dr. Myerson, admitted that nothing in the claims or specification of the '058 or the '971 patents addressed experimental error and that he did not recall any mention of this issue in the file history. *Id*. (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 29:24-33:5; 43:8- 20).

Looking to the claim language, Defendants assert that the precise d-spacing values in the claims and the absence of any modifiers such as "approximately" or "about," indicate that a person skilled in the art would have viewed the recited d-spacing values to be very precise limitations, contrary to Takeda's proposed construction. *Id*. (citing Genck Decl. ¶70).

Defendants argue that the specification of the '058 patent also supports their position, citing Reference Example 4 and Example 2. *Id*. at 9 (citing '058 patent, col. 10, ll. 14-17 (Reference Example 4) and col. 11, l. 55 - col. 12, l. 9 (Example 2)). These examples describe two crystal forms that were made using different methods and were analyzed separately; nonetheless, Defendants point out, "the d-spacings reported for the two crystals are exactly the same, to the hundredth decimal place, with no reported experimental error or other deviation whatsoever." *Id*. According to Defendants, because the inventors provided exact values that were reproducible over multiple experiments, a person skilled in the art would have understood that the claimed d-spacings were meant to be exact values. *Id*. at 10.

Finally, Defendants cite to the claims and specification of the '668 patent in support of their position. *Id*. The '668 patent describes and claims various crystal forms of the enantiomers of lansoprazole and offers multiple experimental examples in which crystal forms of dexlansoprazole are made using various methods. *Id*. (citing Genck Decl. ¶¶ 77-78.). Although these crystals are reported to have different melting properties, the d-spacings that are listed in the examples are exactly the same as the values reported in the '058 patent. *Id*. (citing '668 patent, col. 16, l. 45 - col. 24, l. 5 and comparing '668 patent at col. 18, ll. 44-47, col. 20, ll. 34-38, col.20, ll. 57-61, col. 21, ll. 33-37, col. 21, ll. 60-65, col. 23, ll. 58-62 with '058 patent at col. 10, ll. 14-17, col. 11, l. 55 - col. 12, l. 9). According to Defendants, the precision in these values is particularly striking in light of the fact that different diffraction instruments were used to generate the data in the two patents. *Id*. (comparing '668 patent at col. 16, ll. 14-15 (disclosing a "Rigaku RINT Ultima+" diffractometer) with '058 patent at col. 7, ll. 15-17 (disclosing a "Rigaku RINT2500" diffractometer)). This precision further supports a construction of this claim term that does not incorporate the concept of error, Defendants contend. *Id*.

In response, Takeda points out that Defendants' expert, Dr. Genck, does not dispute that a person skilled in the art at the time of the invention would have understood that the measurement of diffraction peaks using XRPD would have involved a certain amount of experimental error. Takeda Reply Brief on Claim Construction at 2. In particular, in his declaration, Dr. Genck states, "I do not disagree with Dr. Myerson regarding the +/- 0.1 or +/- 0.2 error generally associated with the

two-theta values in normal X-ray powder experiments . . . ." *Id*. (quoting Genck Decl. ¶ 76). Similarly, in his deposition, Dr. Genck testified that there is always some variability in the measurement of diffraction angles. *Id*. (citing Declaration of Erin J. Cox in Support of Takeda's Reply Brief on Claim Construction ("Cox Decl."), Ex. 1 (Genck Dep.) at 98:23-99:8 (testifying that d-spacings measured in any two experiments will be different, "based upon experimental error for the machine") & 105:13-106:22, 108:6-19 (agreeing that as of 1999, a ± 0.1 or a ± 0.2 error rate in the two-theta values was to be expected in a normal X-ray powder experiment)).

Takeda rejects Defendants' reliance on the absence of any reference to experimental error in the claims or specifications of the '058 and '971 patents, arguing that none is necessary because patents are meant to be "a concise statement for persons in the field" and are not drafted for lawyers or judges. *Id*. (citing *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 1119 (Fed. Cir. 2002); *In re Nelson*, 280 F.2d 172, 181 (C.C.P.A. 1960)).

Takeda argues that the identical d-spacings reported in the '058 and '971 patents, cited by Defendants in support of their position that the claims do not incorporate experimental error, "ignores what anyone skilled in the art would know: that measurements made on *different* equipment by *different* operators using *different* samples sizes or sample preparation techniques will necessarily be subject to normal experimental error." *Id*. at 3.

Finally, Takeda challenges Defendants' reliance on the '668 patent in support of their proposed construction, asserting that because the '668 patent has different inventors, a different specification and a different prosecution history than the '058 and '971 patents, it is not intrinsic or relevant extrinsic evidence in determining the meaning of claim terms in the earlier '058 and '971 patents. *Id*. at 2 n. 2.

2. Analysis

As discussed above, the most "significant source of the legally operative meaning of disputed claim language" is the intrinsic evidence of record, that is, the claims, the specification and the prosecution history. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). On the other hand, "[w]hile reference to intrinsic evidence is primary in interpreting claims, the criterion is the meaning of words as they would be understood by persons in the field of the

invention." *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 1119 (Fed. Cir. 2002). In *Verve*, the Federal Circuit explained:

> Patent documents are written for persons familiar with the relevant field; the patentee is not required to include in the specification information readily understood by practitioners, lest every patent be required to be written as a comprehensive tutorial and treatise for the generalist, instead of a concise statement for persons in the field. Thus resolution of any ambiguity arising from the claims and specification may be aided by extrinsic evidence of usage and meaning of a term in the context of the invention.

Id.

The extrinsic evidence here establishes that at the time of the invention, a person skilled in the art would have understood that the values listed in the claims of the '058 and '971 patents, as well as those contained in the examples of the '058 patent, must have allowed for experimental error. All of the cited editions of the USP acknowledge the experimental error associated with XRPD measurements; indeed, *all* of the references cited by the parties in connection with this claim term recognize the experimental error associated with XRPD measurements. Consistent with these references, Defendants' expert conceded in his declaration that there is a " +/- 0.1 or +/- 0.2 error generally associated with the two-theta values in normal X-ray powder experiments." Genck Decl. ¶ 76. Similarly, in his deposition Dr. Genck testified that there is always some experimental error in XRPD diffraction results:

> Q: Is there some probability that if you were to perform X-ray powder diffraction on the same sample ten times, that the d-spacings measured in two of those runs would be identical out to two decimal places?
>
> A: Some probability? I don't know. So – I know that they'd be different, based upon experimental error from the machine . . .
>
> . . .
>
> Q: Do you think there's always some variation in the d-spacings from run to run?
>
> A: By definition there is, yes.

Cox Decl., Ex. 1 (Genck Dep.) at 98-100. In light of this evidence, the Court concludes that a person skilled in the art would not have required any discussion of the experimental error associated with XRPD diffraction, either in the specification or in the claims, to understand that the references to "characteristic peaks at interplanar spacings (d)" allowed for such experimental error.

Nor does the case cited by Defendants, *Callicrate v. Wadsworth Mfg., Inc.*, 427 F.3d 1361, 1368 (Fed. Cir. 2005), support a contrary result. That case merely stands for the proposition that the court may not import limitations from the specification to restrict the claims to coverage of a single embodiment. That is not the situation here, where the Court looks to extrinsic evidence to understand a term that would have been readily understood by a person skilled in the art. Therefore, the Court adopts Takeda's proposed construction.

C. "effective amount" ('971 patent, claim 5)

1. Contentions of the Parties

Takeda's Proposed Construction	Defendants' Proposed Construction
an amount sufficient to help ameliorate or cure reflux esophagitis	the term is indefinite

Claim 5 of the '971 patent claims "a method of treating reflux esophagitis in a mammal in need thereof which comprises administering an effective amount of a crystalline compound of [dexlansoprazole] or a salt thereof, and a pharmaceutically acceptable excipient, carrier or diluent." Although Takeda does not assert claim 5, it asserts dependent claims 6-8, which incorporate the limitations of claim 5. Takeda proposes that the term "effective amount" be construed to mean "an amount sufficient to help ameliorate or cure reflux esophagitis." Defendants assert that this term is indefinite.

Takeda argues in its Opening Claim Construction Brief that the term "effective amount" would be understood by a person skilled in the art to pertain to treatment based on the language of claim 5 (claiming a "method of *treating* reflux esophagitis") and the patent specification (stating that "the crystal of the present invention is useful in mammals . . . for the *treatment* and prevention" of various ailments, including "reflux esophagitis"). Takeda's Opening Claim Construction Brief at 13 (citing '971 patent, col. 3, ll. 54-59) (emphasis added).

Further, Takeda asserts, the term "effective amount" has been found to have a well-established meaning when used in the context of pharmaceuticals: "'[E]ffective amount' is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or

indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation." *Id*. (quoting *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1383-84 (Fed. Cir. 2003)). According to Takeda, the guidance provided in the '971 specification is sufficient to meet this standard because it sets forth a dosage range for treatment of mammals generally, as well as a narrower range for treatment of an adult human. *Id*. (citing '971 patent, col. 4, ll. 19-25). Specifically, the specification states as follows:

> Varying depending on the subject of administration, route of administration, target disease etc., its dose is normally about 0.5 to 1,500 mg/day, preferably about 5 to 150 mg/day, based on the active ingredient, for example, when it is orally administered as an antiulcer agent to an adult human (60 kg). The crystal of the present invention may be administered once daily or in 2 to 3 divided portions per day.

'971 patent, col. 4, ll. 18-24. Takeda contends that a person skilled in the art would understand the meaning of the term "effective amount," as used in claim 5, based on this disclosure. Takeda's Opening Claim Construction Brief at 13 (citing *Schering Corp. v. Mylan Pharms., Inc.*, 2011 WL 3736503 (D.N.J. Aug. 22, 2011) (finding phrase "effective amount" sufficiently definite based on specification's disclosure of dosages); Declaration of Heather Takahashi in Support of Takeda's Opening Claim Construction Brief ("Takahashi Decl."), Ex. B (United States Reissued Patent RE42,461, asserted in *Schering Corp*.) at col. 20, ll. 49-51; col. 20, ll. 64-66 (reflecting dosage range from 1 mg to 1,000 mg/day)).

Takeda also cites to numerous cases in which it asserts the term "effective amount" has been given a construction similar to the one it proposes in this case. *Id*. at 13-14 (citing *Abbott Laboratories v. Baxter Pharmaceutical Products, Inc.*, 334 F.3d 1274 (Fed. Cir. 2003), *Cytomedix, Inc. v. Little Rock Foot Clinic, P.A.*, 2004 WL 1921070, at *4 (N.D. Ill. Aug. 4, 2004); *Teva Pharms. USA, Inc. v. Amgen, Inc.*, 2010 WL 3620203, at *12-13 (E.D. Pa. Sept. 10, 2010); *Medicis Pharm. Corp. v. Acella Pharms. Inc.*, 2011 WL 810044, at *8 (D. Ariz. Mar. 2, 2011); *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 2011 WL 4949042, at *11 (S.D. Cal. Oct. 18, 2011)). Takeda notes that some courts have even concluded that the term needs no construction. *Id*. at 14 (citing *Pfizer Inc. v. Teva Pharms. USA, Inc.*, 803 F. Supp. 2d 397, 408 (E.D. Va. Mar. 17, 2011)).

Defendants do not disagree with Takeda that the "effective amount" term refers to the amount necessary to treat reflux esophagitis in a mammal. Defendants' Claim Construction Brief at

16. They contend, however, that the term is indefinite because a person of ordinary skill in the art would not know from the disclosures of the '971 patent how to determine the "effective amount" to treat "any mammal," as they contend is required by the words of claim 5. *Id*. at 16-18.

First, Defendants argue that the only experimental example disclosed in the '971 patent involves the use of dexlansoprazole to prevent injury of rats' stomachs. *Id*. at 16-17 (citing '971 patent, col. 13, ll. 15-54). According to Defendants' expert, Dr. Triadafilopoulos, this experiment would not have allowed a person skilled in the art to determine the effective amount to treat any mammal because: 1) the experiment involved *prevention* of injury rather than *treatment*; and 2) the experiment focused on injury to the rat's *stomach* and not on injury to or inflammation of the rat's *esophagus*, which would have been the relevant inquiry for treating reflux esophagitis. *Id*. (citing Triadafilopoulos Decl. ¶¶ 33-35).

Second, Defendants assert that the dosage ranges disclosed in the '971 specification at column 4, lines 18-24 also do not provide a sufficient basis for determining the amount necessary to treat any mammal for reflux esophagitis. *Id*. at 17. Defendants point out that the invention of the '971 patent is described as being "useful" for treating a long list of conditions, only one of which is reflux esophagitis. *Id*. (citing '971 patent, col. 3, l. 54 - col. 4, l. 4). Yet, they contend, the dosage ranges in the specification are specific to the use of dexlansoprazole as an "antiulcer agent" and therefore do not offer guidance as to the proper dose to treat reflux esophagitis. *Id*. (citing Triadafilopoulos Decl. ¶ 37). Further, these dosages are insufficient, Defendants assert, because they relate only to the treatment of an adult human, whereas the claim is directed to the treatment of a mammal and the specification lists a wide variety of mammals that can be treated with the claimed invention, including "humans, monkeys, sheep, bovines, horses, dogs, cats, rabbits, rats, mice, etc." *Id*. at 17-18 (citing '971 patent, col. 3, ll. 54-56). Given the differences in the physiology of the gastrointestinal tracts of these different mammals, Defendants contend, the dosages provided for treating gastric ulcers in humans would not provide a person skilled in the art a sufficient basis to determine the appropriate dosages for treating *other* mammals for a different condition, namely, reflux esophagitis. *Id*. at 18 (citing Triadafilopoulos Decl. ¶¶ 30-31, 38-40).

Finally, Defendants assert that the cases cited by Takeda do not stand for a contrary result because in all of them, it would have been possible for a person skilled in the art to determine the dosage that would constitute an "effective amount." *Id*. (citing *Geneva Pharms., Inc. v. GlaxoSmithKline, PLC*, 349 F.3d 1373 (Fed. Cir. 2003)). In particular, Defendants contend that in *Schering Corp. v. Mylan Pharm., Inc.*, *Abbott Labs. v. Baxter Pharm. Prods. Inc.*, and *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, the specification contained "extensive explanations . . . that would allow a skilled artisan to determine the effective amount of the compound at issue." *Id*. Defendants further contend that *Pfizer, Inc. v. Teva Pharms. USA, Inc.* is distinguishable because the court was construing "claims that were aimed at a very specific host and a single disease." *Id*.

In its Reply Brief on Claim Construction, Takeda asserts that Defendants have applied the wrong test: the disclosure is not required to "precisely define the amount of dexlansoprazole sufficient to treat reflux esophagitis" but rather, need only disclose enough information so that a person skilled in the art would be able to determine the amounts required for treatment *without undue experimentation*. Reply Brief on Claim Construction at 3 (citing *Geneva Pharms., Inc. v. GlaxoSmithKline, PLC*, 349 F.3d 1373 (Fed. Cir. 2003)). Defendants, Takeda argues, have not shown by clear and convincing evidence – as is required to establish indefiniteness – that a person skilled in the art would be unable to determine the effective amounts for treatment without undue experimentation. *Id*. (citing *King Pharms., Inc. v. Purdue Pharma L.P.*, 718 F. Supp. 2d 703, 718 (W.D. Va. 2010); *Ortho–McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1365-66 (Fed. Cir. 2008)). Indeed, in another lawsuit, Takeda asserts, Defendant Impax argued that clinical trials did not amount to undue experimentation because the methodology for conducting such trials would have been known to a person skilled in the art. *Id*. at 4 (citing Brief of Plaintiff-Appellant Impax Laboratories, Inc., *Impax Labs., Inc. v. Aventis Pharms. Inc.*, 2005 WL 2598148, at *39-40 (Fed. Cir. filed June 10, 2005)).

Finally, Takeda asserts that the broader of the two dosage ranges provided in the specification – "normally about 0.5 to 1,500 mg/day," depending on the subject of administration and target disease – is sufficient to set out the metes and bounds of the claim and that the inventors were not required to undertake an "impossible task" of specifying exact dosages. *Id*. (citing '971

patent, col. 4, ll. 18-22 & *King Pharms., Inc. v. Purdue Pharma L.P.*, 718 F. Supp. 2d at 718).

2. Analysis

Takeda asks the Court to construe the term "effective amount" as "an amount sufficient to ameliorate or cure reflux esophagitis." Courts have routinely construed the claim term "effective amount" in a manner similar to Takeda's proposed construction. *See, e.g.*, *Cytomedix, Inc. v. Little Rock Foot Clinic, P.A.*, 2004 WL 1921070, at *4 (N.D. Ill. Aug. 4, 2004)(construing "effective amount" as "a sufficient amount of treating composition to facilitate healing"); *Teva Pharms. USA, Inc. v. Amgen, Inc.*, 2010 WL 3620203, at *12-13 (E.D. Pa. Sept. 10, 2010) (construing "administering an effective amount of" as "administering an amount adequate and suitable for therapeutic use"); *Medicis Pharm. Corp. v. Acella Pharms. Inc.*, 2011 WL 810044, at *8 (D. Ariz. Mar. 2, 2011) (construing "effective amount" as "adequate therapeutic dose"); *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 2011 WL 4949042, at *11 (S.D. Cal. Oct. 18, 2011) (construing "effective to treat the chronic lymphocytic leukemia" as "providing a positive clinical benefit to the chronic lymphocytic leukemia patient"). Thus, the Court finds that Takeda's proposed construction adequately captures the meaning of the words "effective amount" as they are used in claim 5.

A more difficult question is whether the term "effective amount" is, nonetheless, indefinite, as Defendants contend. The Federal Circuit has explained that "'effective amount' is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, *provided that* a person of ordinary skill in the art could determine the specific amounts without undue experimentation." *Geneva Pharms., Inc. v. GlaxoSmithKline, PLC*, 349 F.3d at 1383-1384 (emphasis added). Due to the largely factual nature of this inquiry, the Court concludes that this question is more suitable for determination on summary judgment than at the claim construction phase of the case. *See CSB-System Int'l, Inc. v. SAP America, Inc.*, 2011 WL 3240838, at *17-18 (E.D. Pa., July 28, 2011) (discussing reasons for deferring indefiniteness inquiry to summary judgment). Accordingly, the Court adopts Takeda's proposed construction without prejudice to Defendants' bringing a motion for summary judgment on the question of whether the standard set forth in *Geneva Pharmaceuticals* is met as to the claim term "effective amount."

D. "melting start temperature" ('668 patent, claims 9 and 10)

1. Contentions of the Parties

Takeda's Proposed Construction	Defendants' Proposed Construction
the temperature at which crystals start to melt, represented by the onset temperature of melting as measured by differential scanning calorimetry	the term is indefinite

Claim 9 of the '668 patent claims a crystal "having a melting start temperature of not lower than about 131° C." Claim 10 is dependent on claim 9, claiming "[t]he crystal from claim 9, wherein the melting start temperature is about 135° C." Takeda proposes that the term "melting start temperature" should be construed to mean "the temperature at which crystals start to melt, represented by the onset temperature of melting as measured by differential scanning calorimetry." Defendants argue that the term is indefinite.

In its Opening Claim Construction Brief, Takeda argues that the term "melting start temperature" is defined in the specification of the '668 patent, which states that "[a]s used herein, the 'melting start temperature' refers to the temperature at which crystals start to melt when heated under, for example, the DSC measurement conditions to be mentioned below." Takeda Opening Claim Construction Brief at 15 (citing '668 patent, col. 12, ll. 4-7). Further, Takeda points out, the specification sets out the specific DSC conditions under which "melting start temperature" can be measured in the specification, stating as follows:

> The melting start temperature was measured using DSC (differential scanning calorimeter SEIKO DSC220C) under the following measurement conditions.
>
> DSC Measurement Conditions;
>
> temperature range: room temperature to 220° C.
>
> temperature rise rate: 0.5° C./min.
>
> sample container: aluminum pan (without cover)
>
> atmosphere: nitrogen gas (100 mL/min)

Id. (quoting '668 patent, col. 16, ll. 15-22).

The extrinsic evidence also shows that a person skilled in the art at the time of the invention[6] would have been familiar with the concept of the "melting start temperature," Takeda asserts. *Id*. at 16. In particular, Takeda cites the 1995 and 2005 editions of the United States Pharmacopeia. *Id*. The 1995 version provided that, for thermal analysis measurements performed by heating a substance in a glass tube, "[t]he temperature at which the column of the substance under test is observed to collapse definitely against the side of the tube at any point is defined as the beginning of melting." Myerson Decl. ¶ 73 & Ex. 22 ("Melting Range or Temperature," The United States Pharmacopeia, 1805-06 (25th rev. 1995) at DEX0014733). The 2005 edition additionally provided that, when a heat phase test is performed using an apparatus having a detector signal to monitor the melting process, the "beginning of melting" is defined as "the temperature at which the detector signal first leaves its initial value." Myerson Decl., Ex. 23, at DEX0014750 ("Melting Range or Temperature," The United States Pharmacopeia, 2433-34 (28th rev. 2005)). The 2005 edition elsewhere notes that "'onset'. . . temperature can be determined objectively and reproducibly, often to within a few tenths of a degree." Myerson Decl. ¶ 73 & Ex. 24, at DEX0014754 ("Thermal Analysis," The United States Pharmacopeia, 2501-03 (28th rev. 2005)).

Defendants assert that the term "melting start temperature" did not have a generally understood meaning to persons skilled in the art at the time of the invention, rejecting both the extrinsic and intrinsic evidence cited by Takeda. Defendants' Claim Construction Brief at 11. With respect to the extrinsic evidence, Defendants argue that the references cited by Takeda provided disparate definitions of various melting terms, both generally and in the context of measurements using the DSC method. *Id*. Defendants point out that the 1995 United States Pharmacopeia defines the "beginning of melting" when using the capillary method as "[t]he temperature at which the column of substance under test is observed to collapse definitely against the side of the tube at any point," and the "end of melting" (which it equates with the "melting point") as "the temperature at which the test substance becomes liquid throughout." *Id*. (citing Myerson Decl., Ex. 22 ("Melting

[6]Takeda contends that the relevant date in this respect is December 1, 2000, the date of filing of the Japanese Patent application upon which the '668 patent was based. Defendants do not challenge this assertion.

Range or Temperature," The United States Pharmacopeia, 1805-06 (25th rev. 1995)) at DEX0014733; Jorjani Decl., Ex. 1 (Myerson Dep.) at 49). Further, Defendants point out, these two temperatures are said to fall within the "melting range." *Id*. (citing Myerson Decl., Ex. 22 at DEX0014733; Jorjani Decl., Ex. 1 (Myerson Dep.) at 52:16-21 ("All melting points are reported as a range")).

In contrast, in the context of the DSC method, Defendants point out, extrinsic evidence cited by Takeda in its joint claim construction chart defines the "melting point" as the point at which the DSC curve leaves the baseline, without providing any range of temperatures. *Id*. at 11-12 (citing Genck Decl. ¶ 84 & Ex. 4 (Brown, M.E., "Determination of Purity by Differential Scanning Calorimetry," *J. Chem. Ed.* 1979, 310-313) at DEX00144954). According to Defendants, another article cited by Takeda in support of its proposed construction equates the "melting point" with the "onset temperature," while yet another defines the "onset temperature" as the intersection of the slope of the DSC baseline and the slope of the relevant peak in the DSC curve. *Id*. at 12 (citing Genck Decl., Ex. 5 (D'Amelia, R. *et al*., "Introduction of Differential Scanning Calorimetry in a General Chemistry Laboratory Course: Determination of Thermal Properties of Organic Hydrocarbons," *J. Chem. Ed.*, 2007, 84(3), 453-455) at DEX0014506); Myerson Decl., Ex. 10 (Hancock and Zografi) at DEX0014587; Genck Decl. ¶ 85 & ¶ 94 n.9).

Defendants also cite to the deposition testimony of Dr. Myerson, in which Dr. Myerson allegedly confirmed that there was no uniform definition for "melting start temperature." *Id*. at 12 (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 49:10-55:7, 58-61, 75-78, 82-85)(conceding that references cited by Takeda in support of proposed construction do not use exact term "melting start temperature").

Regarding the intrinsic evidence, Defendants contend that the definition in the specification cited by Takeda (defining the melting start temperature as the "temperature at which crystals start to melt") would not have offered any guidance because it is circular. *Id*. at 12. Further, Defendants assert, the definition of "melting start temperature" offered in the specification is not limited to any particular method of measuring, as is clear from the fact that the DSC method is offered only as an "example." *Id*. at 13 (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 63-65).

Defendants also cite to the prosecution history in support of their position that this claim term is indefinite. *Id*. at 13. Specifically, Defendants cite to a declaration submitted during prosecution stating that the crystals of '058 Examples 1 and 2 have a "melting start temperature" of 128.3º C and 129.1º C, respectively, using the DSC method. *Id*. (citing Myerson Decl., Ex. 21 (Declaration of Tadashi Urai)). Defendants note that the '058 patent reports a melting range of 144.0º C to 144.5º C and 147.0º C to 148.0º C, respectively, for the same crystals, using a "Micro Melting Point Apparatus." *Id*. (citing '058 patent, col. 10, l. 44, col. 11, l. 44, col. 6, ll. 61-63). Thus, Defendants assert, despite the fact that the lower ends of the melting ranges are reported in the '058 patent as 144.0º C (Example1) and 147.0º C (Example 2), the inventors told the patent office that the "melting start temperatures" for the same crystal were actually 128.3 º C and 129.1º C. According to Defendants, this disparity suggests that either the same crystals can have widely varying "melting" characteristics based on the analytical method used, or the '668 inventors used the term "melting start temperature" to mean something entirely different than what, according to Takeda's expert, the "start of melting" meant to a skilled artisan. *Id*. (citing Genck Decl. ¶¶ 88-89). Further, Defendants argue, Dr. Myerson had "no credible explanation for this huge temperature difference" when questioned about it at his deposition. *Id*. (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 94:17-101:20).

In its Reply Claim Construction Brief, Takeda argues that Defendants have attempted to obfuscate the issue by focusing on definitions of terms that are irrelevant to the claim term in question, such as "end of melting," "melting point" and "melting range," and by referring to methods of measuring melting temperature that are not mentioned in the '668 patent. Takeda's Reply Brief on Claim Construction at 5. The specification of the '668 patent provides both a method for measuring melting start temperature and a clear definition of the term, Takeda asserts. *Id*. In particular, Takeda cites to the following excerpt of the specification:

> The crystal obtained by the above-mentioned production method (step (1) alone, or step (2) after step (1)) *has the following melting start temperature by DSC measurement (temperature rise rate 0.5° C./min). . . . The crystal has the melting start temperature of not less than about 131° C.*, preferably about 131° C. to about 137° C., more preferably about 132° C. to about 135° C., most preferably about 133° C. to about 135° C., particularly preferably about 135° C.

Id. (quoting '668 patent, col. 12, ll. 1-12 (emphasis added by Takeda)). Thus, Takeda contends, a person skilled in the art would understand that "melting start temperature," as used in claims 9 and 10, was to be measured using differential scanning calorimetry ("DSC"), and not using the other techniques discussed by Defendants in their brief. *Id*.

Takeda further points out, as it did in its Opening Claim Construction Brief, that the '668 specification defines "melting start temperature" as "the temperature at which crystals start to melt when heated under, for example, the DSC measurement conditions to be mentioned below." *Id*. (citing '668 patent, col. 12, ll. 5-7). According to Takeda, a person skilled in the art would have understood this definition because, at the time of the invention, such a person would have understood how to use DSC to measure "the temperature at which crystals start to melt." *Id*. at 5. In particular, Takeda contends, a person skilled in the art knew that in DSC analysis, the melting of a pure crystalline solid produces a peak on the DSC heat flow plot, that the entire peak represents the heat of melting, and that the point where the heat flow curve departs from the baseline is the start of melting. *Id*. at 5-6 (citing Genck Decl. ¶ 40 & fig., Ex. 7, at 2390 & fig.1 (example of a heat flow curve); Myerson Decl. ¶ 43 & fig.1; Cox Decl., Ex. 1 (Genck. Dep.) at 43:25-44:11, 45:4-23 (admitting that the point where the heat flow curve departs from the baseline is sometimes called the onset of melting), Ex. 3 (Myerson Dep.) at 70:4-74:19 & Ex. 4 (Genck Dep. Ex. 21) at 82-83 & fig.5.2 (excerpt of book entitled "Differential Scanning Calorimetry," published in 1996, describing the point where the curve of measured values begins to deviate from the baseline as the "initial peak temperature")).

Takeda also points to extrinsic evidence in support of its position. In addition to the 2005 edition of the United States Pharmacopeia, cited in its Opening Claim Construction Brief, Takeda cites to two references that were offered as exhibits during Dr. Genck's deposition. *Id*. at 6. The first is a European Patent Application in which the term "melting start temperature" is defined as "a temperature at which the DSC leaves the line obtained by extending a base line to the high temperature side"). *Id*. (citing Cox Decl., Ex. 5 (Genck Dep. Ex. 23), European Patent Application No. EP 0990513 ("the '513 application"), published on April 5, 2000, at [0041]). The second is a European Patent defining "melting start temperature" as "the temperature at the intersection of the

differential thermal curve and the extended line of the base line on the high temperature side from the maximum peak to the low temperature side." *Id*. (citing Cox Decl., Ex. 6 (Genck Dep. Ex. 24) (European Patent No. EP 1223474 (the "'474 patent"), granted on February 20, 2008, at [0042])).

In light of this intrinsic and extrinsic evidence, Takeda asserts, a skilled artisan would have understood the meaning of "melting start temperature" as the term was used in claims 9 and 10 of the '668 patent. *Id*. Further, Takeda argues, such a person would have understood that "melting start temperature" would be measured using DSC and would have known how to obtain those melting start temperatures. *Id*. Therefore, Takeda argues, the term is not indefinite. *Id*. (citing *Marley Mouldings Ltd. v. Mikron Indus., Inc.*, 417 F.3d 1356, 1360-61 (Fed. Cir. 2005) ("§ 112 ¶ 2 is satisfied when the relevant values can be 'calculated or measured.'")).

Impax has filed a surreply responding to three references that were offered by Takeda in support of its proposed construction for the first time in its Reply Claim Construction Brief. Impax Claim Construction Surreply at 2 (citing Cox Declaration, Exhibits 4, 5 and 6). Impax argues that these documents, rather than supporting Takeda's position, show that the term "melting start temperature" is indefinite.[7] *Id*. As to the '513 application and the '474 patent, Impax argues that "[t]he fact that each of these patent documents specifically defines 'melting start temperature' demonstrates that this term had no well-understood meaning to persons of skill in the art at the time the '668 patent was filed." *Id*. at 3. Further, Impax asserts, to the extent Takeda relies on these references, it is attempting to improperly import a definition of the term "melting start point" from unrelated patents. *Id*. (citing *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1318 (Fed. Cir. 2005)). According to Impax, Takeda admits that this is improper in footnote 2 of its reply brief, where it challenges Defendants' reference to the '668 patent in relation to the construction of the "characteristic peaks" claim term. *Id*. (citing Takeda Reply Brief on Claim Construction at 2, n.2).

Impax also rejects Takeda's reliance on the 1996 book entitled "Differential Scanning Calorimetry." *Id*. at 4 (citing Cox Decl., Ex. 4). According to Impax, this publication further illustrates that the term "melting start temperature" had no well-understood meaning in the art at the

[7]Although Impax contends that Takeda should have disclosed these references in its opening brief, it does not ask the Court to exclude the documents.

time of the '668 invention. In particular, the passage cited by Takeda defines the point where the curve of measured values begins to deviate from the baseline as the "initial peak temperature." *Id.* (citing Takeda Reply Brief at 5-6). Thus, Impax asserts, this document "assigns yet a different name to the point at which the DSC curve leaves the baseline: it does not refer to it as the 'onset,' contrary to Takeda's claim construction, and it does not refer to it as the 'melting start temperature,' contrary to Takeda's insistence that the '668 patent must have meant the same thing by its use of this term." *Id.* According to Impax, because "the '668 patent used a term coined by its own inventors, 'melting start temperature,' that is not used in any reference book or generally understood to have any particular meaning," the claim term is indefinite. *Id.*

2. Analysis

Defendants contend that a person skilled in the art would not have discerned the boundaries of claim 9 of the '668 patent because the term "melting start temperature" was not a term that had a set meaning at the time of the invention and could have had a number of different meanings, depending upon the thermal measurement techniques used. Even if it would have been understood that the term referred to DSC, Defendants assert, it is not clear what point on the DSC peak the term referred to. The Court rejects both contentions.

First, the extrinsic evidence supports the conclusion that the concept of a "melting start temperature" would have been understood by a person skilled in the art at the time of the invention. Both the 1995 and the 2005 versions of the United States Pharmacopeia discuss the "beginning of melting," and the 2005 Pharmacopeia states that in the context of DSC, "an 'onset' . . . temperature can be determined objectively and reproducibly, often to within a few tenths of a degree." Myerson Decl., Ex. 22 (1995 version of United States Pharmacopeia at 1805), Ex. 23 (2005 version of United States Pharmacopeia at 2433-2434), Ex. 24 (2005 Version of United States Pharmacopeia at 2502). Further, Takeda's expert has testified that in this context, "beginning" and "onset" are synonymous with "start." *See* Jorjani Decl., Ex. 1 (Myerson Dep.) at 51, 52, 55, 85.

Second, a person skilled in the art would have understood from the '668 specification that the "melting start temperature" in claim 9 of the '668 patent referred to the melting start temperature

that would be obtained using DSC measurement. Most significantly, the '668 specification states as follows:

> The crystal obtained by the above-mentioned method . . . has the following melting start temperature by DSC measurement . . . As used herein, the "melting starting temperature" refers to the temperature at which crystals start to melt when heated under, for example, the DSC measurement conditions to be mentioned below.

'668 patent, col. 12, ll. 1-7. The most natural reading of this portion of the specification is that "melting start temperature" is determined using DSC measurement; the words "for example" refer to the specific DSC measurement conditions described later in the specification as an example of the DSC measurement that is referred to generally in the previous sentence. This interpretation is consistent with the fact that the '668 specification refers *only* to DSC as a method for measuring the melting starting point. Thus, Dr. Myerson opined that "if one was attempting to reproduce the teachings of the ['668] patent, . . . one of ordinary skill would be led to the use of DSC for such a measurement." Cox Decl., Ex. 3 (Myerson Decl.) at 64-65. Accordingly, the Court rejects Defendants' assertion that the term "melting start temperature," as used in claim 9, would have been insolubly ambiguous to a person skilled in the art. Rather, it would have been apparent that the term referred to the beginning – or onset – of melting as measured by DSC.

The Court next turns to the question of whether the term "melting start temperature" is indefinite because a person skilled in the art at the time of the invention would not have known *where* on the DSC curve the onset of melting occurred. While the '668 patent specification does not offer significant guidance on this question, the extrinsic evidence supports the conclusion that a person skilled in the art would have understood that the melting start point using DSC is the point where the heat flow curve departs from the baseline. This definition is consistent with the definition of a very similar term, "the beginning of melting," that is provided in the 2005 edition of the United States Pharmacopeia, stating that "[t]he temperature at which the detector signal first leaves its initial value is defined as the beginning of melting." Myerson Decl., Ex. 23 (United States Pharmacopeia, 28th rev. (2005)) at DEX0014750. Similarly, figure 5.2 of the book Differential Scanning Calorimetry refers to this point as the "*initial* peak temperature." *See* Cox Decl., Ex. 4 at 82. Further, the '513 application and the '474 patent explicitly define "melting start temperature"

with reference to this point.

The Court is not persuaded by Defendants' assertion that there are "multiple points on a DSC curve at which melting could be said to begin" and that the use of the word "onset" in Takeda's proposed construction is arbitrary. *See* Genck Decl. ¶ 94. In support of this point, Defendants cite Dr. Genck's opinion that the word "onset" refers to "the point of intersection of the tangent drawn at the point of greatest slope on the leading edge of the peak . . . with the extrapolated baseline." Genck Decl. ¶ 94 & n. 9 (citing Genck Decl., Ex. 7 (IUPAC Article) at 2390; Genck Decl., Ex. 8 (IUPAC website) at 4). The point referenced by Dr. Genck, however, is used in all of the cited references with the modifier "extrapolated." In particular, the IUPAC references cited by Dr. Genck reflect that the definition he provides is for the term "extrapolated onset." *Id*. Similarly, fig. 5.2 of Differential Scanning Calorimetry refers to this point as Te, or "*extrapolated* peak onset temperature." Cox Decl., Ex. 4 at 82 (emphasis added). The '668 patent, however, contains nothing suggesting that the inventors intended that the melting start temperature referred to this *extrapolated* onset temperature. Nor does Takeda's proposed construction incorporate this term.

The Court also rejects Impax's contention that the inclusion of definitions of "melting start temperature" in the '513 application and the '474 patent shows that the term did not have an established meaning at the time of the invention. The fact that other inventors chose to provide an explicit definition of the same term in unrelated patent applications gives rise to, at best, only a weak inference that the term "melting start temperature" might not have had an established meaning at the time of the invention. That inference is insufficient to establish that the term is indefinite, particularly in light of the extrinsic evidence cited above.

Based on the intrinsic and extrinsic evidence cited by Takeda, the Court finds that the claim term "melting start point" is not indefinite and adopts Takeda's proposed construction of that term.

E. "about" ('668 patent, claims 9 and 10)

1. Contentions of the Parties

Takeda's Proposed Construction	Defendants' Proposed Construction
Plain and ordinary meaning, ie., approximately	With a variation of no more than 0.5°C Accordingly, "about 131° C" includes temperatures between 130.5° C and 131.5° C, and "about 135° C" includes temperatures between 134.5° C and 135.5° C

Claims 9 and 10 of the '668 patent cover a crystalline compound whose melting start temperature is "not lower than about 131° C," and "about 135° C," respectively. Takeda argues that the term "about" should be given its plain and ordinary meaning of "approximately." Defendants contend that the term should be construed to mean "with a variation of no more than 0.5° C. Under that construction, "about 131° C" would include temperatures between 130.5° C and 131.5° C, and "about 135° C" would include temperatures between 134.5° C and 135.5° C.

In its Opening Claim Construction Brief, Takeda argues that because neither the specification nor the prosecution history of the '668 patent indicates the range of values the word "about" is intended to encompass, the term should simply be given its plain and ordinary meaning, that is, "approximately." Takeda's Opening Claim Construction Brief at 17 (citing *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995); Myerson Decl. ¶¶ 76-78). Takeda contends that this approach is consistent with Federal Circuit precedent, which explains that where a claim is drafted "using terminology that is not as precise or specific as it might be," the court should construe the claim with "whatever specificity is warranted by the language of the claim and the evidence bearing on the proper construction" but should not go further, under the rubric of claim construction, by providing *additional* specificity in order to facilitate a comparison of the claim and the accused product. *Id*. (citing *PPG Indus. v. Guardian Indus. Corp*., 156 F.3d 1351, 1355 (Fed. Cir. 1998)). Takeda also cites district court cases in which courts have declined to specify a particular range in connection with the claim term "about" and instead have construed the term to mean "approximately." *Id*. at 18 (citing *Biopolymer Eng'g Inc. v. Immunocorp*., 2007 WL 4562592, at *10 (D. Minn. Dec. 21, 2007) ("[w]ithout evidence that would provide a basis to specify

the permissible deviation from one percent, the Court gives the term 'about' its ordinary meaning of 'approximately'"); *Unigene Labs., Inc. v. Apotex Inc.*, 2008 WL 3992294, at *4, *9 (S.D.N.Y. Aug. 28, 2008) (where term "about" was "used in all the claims to indicate an approximate measurement of a substance," and "nothing in the patent specification contradict[ed] this ordinary and customary meaning," court construed the word "about" in phrase "about 20 mM citric acid" to mean "approximately" and "construe[d] the claim term no further")).

Defendants argue that the term "about" should be construed more specifically to identify the degree of variation the term permits in the claimed melting start temperature. Defendants' Claim Construction Brief at 15. In support of their position, Defendants cite Dr. Myerson's deposition testimony, in which he stated that "about 135° C" in claim 10 of the '668 patent" would allow for a variation of ".2, .3 degrees C maximum," in light of his conclusion that the claimed "melting start temperature" would be measured with DSC and based on how a person of ordinary skill in the art would understand DSC works. *Id*. (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 106).

Defendants further contend that the '668 claims and specification support their position. *Id*. As to the claims, Defendants point to the opinion of their expert, Dr. Genck, that because no error bars or standard deviations are provided following the temperatures recited in the claims, a person of ordinary skill in the art would understand that the recited figures result from rounding the experimental results up or down using "normal arithmetic conventions." *Id*. at 16 (citing Genck Decl. ¶ 99). As to the specification, Defendants argue that a variation of half a degree is consistent with the experimental examples for dexlansoprazole, in which every "melting start temperature" disclosed for dexlansoprazole is reported to an accuracy of no more than half of a degree. *Id*. (citing '668 patent at col. 18, l. 54, col. 20, l. 44, col. 20, l. 67; '058 patent at col. 21, l. 47, col. 22, ll. 4, 15, 29, 41, 56, col. 23, ll. 4, 19, 33, col. 24, l. 5; Genck Decl. ¶ 100).

Finally, Defendants argue that the extrinsic evidence cited by Takeda is consistent with their proposed construction to the extent that these references allow for a variation of between a few tenths of a degree Celsius up to half a degree. *Id*. In particular, Defendants' expert, Dr. Genck, notes that the 2005 United States Pharmacopeia states that melting temperatures as measured by DSC "can be determined objectively and reproducibly, often to within a few tenths of a degree" and

further states that "[m]elting-point determinations by scanning calorimetry have a reproducibility with a standard deviation of about 0.2º C." Genck Decl. ¶ 102 (citing Myerson Decl., Ex. 24 at DEX0014754- 14755). Defendants also cite to another reference stating that measurements of these temperatures have "[d]eviations as small as 0.02º C to 0.1º C" and should be reported "to the nearest 0.1º C (or at least 0.5º C) for routine melting point ranges." *Id*. at 16 (citing Genck Decl., Ex. 6)(Stanford Research Systems, "Melting Point Determination") (cited by Takeda in Docket No. 52 (Joint Claim Construction and Prehearing Statement), Appendix B in support of proposed construction of "melting start temperature") at DEX0014703, DEX0014711).

In its Reply Claim Construction Brief, Takeda argues that if the Court is inclined to specify a particular degree of variation associated with the term "about," it should specify a narrower range of no more than 0.2 °C to 0.3 °C on the low end in light of the fact that the difference between melting start points of the prior art crystals and the crystal of the '668 patent is less than 2° C. Reply Claim Construction Brief at 6-7 (citing Myerson Decl., Ex. 21 (Declaration of Tadashi Urai, Sept. 6, 2005) at DEX0003569)).[8] Takeda also cites to the 2005 version of the United States Pharmacopeia, which states that DSC measurements have a standard deviation of 0.2 °C . *Id*. (*citing* Myerson Decl., Ex. 24 at DEX0014755).

2. Analysis

"[T]he word 'about' does not have a universal meaning in patent claims, and . . . the meaning depends on the technological facts of the particular case." *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995) (citation omitted). In *Pall Corp*., the Federal Circuit offered the following guidance for construing this claim term:

> The use of the word "about," avoids a strict numerical boundary to the specified parameter. Its range must be interpreted in its technologic and stylistic context. We thus consider how the term . . . was used in the patent specification, the prosecution history, and other claims. It is appropriate to consider the effects of varying that parameter, for the inventor's intended meaning is relevant. Extrinsic evidence of meaning and usage in the art may be helpful in determining the criticality of the parameter, and may be received from the inventor and others skilled in the field of the invention.

[8] This declaration was submitted to the patent office by one of the '668 inventors, Tadashi Urai, in support of the '668 application. In it, he provides the melting start temperatures for three prior art crystals, described as examples in U.S. Patent No. 6462058, which he obtained using DSC. The three temperatures are as follows: 128.7 °C (Example 4), 128.3 °C (Example 1) and 129.1 °C (Example 2).

Id. Where courts have found that the intrinsic evidence does not offer sufficient guidance to determine a specific range, the word "about" has been given its plain and ordinary meaning, that is, "approximately." *See, e.g., Biopolymer Engineering, Inc. v. Immunocorp*, 2007 WL 4562592, at *10 (D. Minn. Dec. 21, 2007); *Unigene Labs., Inc. v. Apotex Inc*., 2008 WL 3992294, at *4, *9 (S.D.N.Y. Aug. 28, 2008).

The Court finds that the intrinsic evidence cited by the parties in this case offers insufficient guidance to construe the term "about" with reference to a specific temperature range. The intrinsic evidence does not allow the Court to determine a specific range because while the specification indicates that a person skilled in the art would have understood that the claimed temperatures were measured using DSC – which was capable of determination to within "a few tenths of a degree" – the temperatures in the asserted claims are stated without any error bars or standard deviations, suggesting that "about" might permit a broader range of temperatures. As a result, any inference based on the specification that "about" indicates a specific range associated with the accuracy of DSC measurements is undercut by the claims themselves. Under these circumstances, it is inappropriate to assign a specific range to the term "about."

Accordingly, the Court finds that the term "about" means "approximately."

F. "amorphous compound" ('282 patent, claims 1 and 2)

1. Contentions of the Parties

Takeda's Proposed Construction	Defendants' Proposed Construction
A non-crystalline solid that lacks the long-range order characteristic of a crystal	Plain meaning

Claims 1 and 2 of the '282 patent recite the term "amorphous compound" of dexlansoprazole. Defendants assert that this term should be given its plain and ordinary meaning, that is, a compound that is amorphous, or non-crystalline in form. Takeda proposes that the term be construed as "a non-crystalline solid that lacks the long-range order characteristic of a crystal." The primary dispute between the parties is whether the term is limited to solids or rather, includes liquids or oils that are amorphous.

In support of its proposed construction, Takeda cites numerous references that distinguish between amorphous and crystalline compounds. Takeda Opening Claim Construction Brief at 19 (citing Myerson Decl. ¶¶ 80-81). Some of these references are cited only to show that an "amorphous compound" lacks long range order. *See* Myerson Decl., Ex. 10, at DEX0014581 (Hancock and Zografi); *id.*, Ex. 11, at DEX0014516 (S.R. Elliott, Physics of Amorphous Materials, 6 (2d ed. 1990)) ("amorphous materials do not possess the long-range translational order (periodicity) characteristic of a crystal"). Others offer definitions of amorphous *solids*, but do not directly address whether an "amorphous compound" must be a solid. *See id.*, Ex. 26, at DEX0014494 (Theodore L. Brown et al., Chemistry, The Central Science, G-1 (8th ed. 2000)) (defining "amorphous solid" to mean "a solid whose molecular-arrangement lacks a regular long-range pattern"); *id.*, Ex. 13, at DEX0014770 (Richard Zallen, The Physics of Amorphous Solids 1-5 (2004)) ("in amorphous solids, long-range order is absent; the array of equilibrium atomic positions is strongly disordered"); *id*., Ex. 27, at DEX0014491 (James E. Brady and Fred Senese, Chemistry: Matter and Its Changes, G-1 (4th ed. 2004)) (defining "amorphous solid" as "a noncrystalline solid"). Finally, two of the references cited in Takeda's opening brief suggest that an "amorphous compound" would have been understood by a person of skill in the art to mean a solid. *See id*., Ex. 12, at DEX0014612 (Allan S. Myerson and Rajiv Ginde, Crystals, Crystal Growth, and Nucleation, in Handbook of Industrial Crystallization 33 (2d ed. 2002)) ("Materials that have short-range order rather than long-range ordering, like glass, are non-crystalline solids. A noncrystalline solid is often referred to as an amorphous solid"); *id*., Ex. 14, at DEX0014719 (Hsien-Hsin Tung et al., Crystallization of Organic Compounds: An Industrial Perspective 25 (2009)) (hereinafter, "Hsien-Hsin Tung") ("amorphous materials are solids in which molecules do not have a periodical three-dimensional pattern").

Takeda further asserts that the term "amorphous compound" refers to a *solid* based on the two examples in the '282 patent specification that use the term "amorphous substance," Reference Examples 1 and 2. *Id*. at 19-20 (citing Myerson Decl. ¶¶ 83-84). Takeda's expert explains as follows:

> Reference Examples 1 and 2 describe the isolation of optically pure dexlansoprazole from a starting material consisting of racemic lansoprazole (containing both the right and left enantiomers). The specification states that the isolated dexlansoprazole was "evaporated to dryness to yield R(+)-lansoprazole . . . as an amorphous substance." '282 patent, col. 8, ll. 3-6; '282 col. 8, ll. 25-29. This reference to drying the amorphous substance indicates that the amorphous substance was in a solid form.

Myerson Decl. ¶ 83.[9]

Takeda further asserts that the comparison in Reference Example 2 of the stability of the amorphous form of dexlansoprazole to the crystal form supports the conclusion that "amorphous compound" means "amorphous solid," citing the following description in the '282 specification:

> The crystals of R(+)-lansoprazole as obtained in Example 2 (about 5 mg) and amorphous R(+)-lansoprazole as obtained in Reference Example 1 (about 5 mg) were each taken in a colorless glass bottle, and their stability during storage at 60° C. (stopper removed) was examined. A 25 ml solution (concentration: about 0.2 mg/ml) of the sample after completion of storage in the mobile phase, along with a standard solution prepared using the initial lot, was analyzed under the HPLC conditions shown below, and the R(+)-lansoprazole content (residual percentage) was calculated from the peak area obtained. . . .
>
> When the sample was stored at 60° C. (exposed), the crystal of Example 2 retained a content exceeding 90% for up to 4 weeks, whereas the amorphous form of Reference Example 1 showed reduction in content to 70.8% after 1 week and 57.5% after 2 weeks. This finding demonstrates that the crystal of R(+)- lansoprazole is more stable and more preferable for use as a pharmaceutical etc. than the amorphous form.

Takeda Claim Construction Brief at 20 (citing col. 14, ll. 4-14, 41- 47). According to Takeda, because crystals are solid substances, a person skilled in the art would understand that a stability test comparing an amorphous compound to a crystalline compound would involve a comparison of like to like, that is, a solid to a solid. *Id*. (citing Myerson Decl. ¶ 84).

Finally, Takeda contends that construction of the term "amorphous compound," like "crystal" and "crystalline compound," will be helpful to the Court because it "elucidates in an empirically verifiable way the differences in molecular structure that distinguish an amorphous compound, on the one hand, from a crystalline compound, on the other." *Id*.

Defendants argue that no construction of the claim term "amorphous compound" is necessary and further, that Takeda is seeking to improperly import a limitation into the claims by limiting the

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[9]At his deposition, Dr. Myerson expanded on his opinion that the reference to evaporation indicated a solid, explaining that "if somebody produces an oil in an example, they say an oil. If they produce an amorphous solid, they would normally say an . . .amorphous substance." Jorjani Decl., Ex. 1 (Myerson Dep.) at 164.

term to a solid without a clear indication that the patentees intended to restrict the meaning of the claim term in this manner. Defendants' Claim Construction Brief at 19 (citing *Callicrate v. Wadsworth Mfg., Inc*., 427 F.3d 1361, 1368 (Fed. Cir. 2005); *Epistar Corp. v. ITC*, 566 F.3d 1321, 1334-1335 (Fed. Cir. 2009) & *Teleflex, Inc. v. Ficosa N. Am. Corp*., 299 F. 3d 1313, 1327-1328 (Fed. Cir. 2002)).

According to Defendants, when the '282 patent application was originally filed, in 1999, a person of ordinary skill in the art understood that "amorphous" meant "non-crystalline," that a "compound" included both solids and nonsolids, and that an "amorphous compound" could exist in different physical forms such as solids, liquids and oils. *Id*. (citing Expert Declaration of Robin D. Rogers in Support of Handa Pharmaceuticals, LLC's Opening *Markman* Brief ("Rogers Decl.") ¶¶ 27-32). Dr. Rogers cites three references in support of this conclusion. First, he cites a dictionary that defines "amorphous substance" as "a substance in which its constituent basic particles (ions, atoms, molecules) are not regularly distributed" and states further that "[p]lasmas, gases and liquids are always in an amorphous state." Rogers Decl. ¶ 27 & Ex. 3 (Comprehensive Dictionary of Physical Chemistry L. (Ulicky & T.J. Kemp ed., Ellis Horwood) (1992) (hereinafter, "Ulicky") at page 21 (DEX0003649)).

Second, he cites a dictionary that defines "amorphous" as follows:

> noncrystalline, having no molecular lattice structure which is characteristic of the solid state. All liquids are amorphous. Some materials that are apparently solid, such as glasses, or semisolid, such as some high polymers, rubber and sulfur allotropes, also lack a definite crystal structure and a well-defined melting point. They are considered high viscosity liquids.

Rogers Decl. ¶ 28 & Ex. 4 (Hawley's Condensed Chemical Dictionary, 15th Ed., (Richard J. Lewis ed., John Wiley & Sons, Inc. (2007), at page 75 (IPXL-000902)).

Third, he cites an encyclopedia of science and technology that defines "amorphous solid" as follows:

> A rigid material whose structure lacks crystalline periodicity; that is, the pattern of its constituent atoms or molecules does not repeat periodically in three dimensions. In the present terminology amorphous and noncrystalline are synonymous. A solid is distinguished from its other amorphous counterparts (liquids and gases) by its viscosity.

Rogers Decl. ¶ 29 (citing Myerson Decl., Ex. 15 (McGraw-Hill Concise Encyclopedia of Science and Technology, 3rd Ed., (Sybil P. Parker, ed. McGraw-Hill Book Company) (1994) at pages 84-85 (IPXL-0009907-08))).

Further, Defendants contend, the '282 patent does not contain an express disavowal of non-solid amorphous compounds or any express definition limiting "amorphous compound" to "non-crystalline solids." *Id*. at 19-20 (citing Rogers Decl. ¶¶ 33-45). Defendants note that at his deposition, Dr. Myerson agreed that the '282 patent does not define the term "amorphous compound" or expressly disavow nonsolid amorphous compounds and further, that a person skilled in the art would understand the term to encompass solid and nonsolid compounds if it were interpreted "without reference to the specification at all . . . in a vacuum." *Id*. at 20 (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 132:23-133:3; 133:16-134:4; 136:12-24; 137:13-23; 144:4-13; 146:16-21)).

Addressing the references cited by Dr. Myerson in support of Takeda's proposed construction, Defendants contend that only two of the references existed at the time of the invention, in 1999, namely, the Hancock and Zografi reference and the Elliot reference. *Id*. at 20 (citing Myerson Decl. ¶ 81 & Exs. 10, 11). These references, Defendants assert, do not support Takeda's position because they define "amorphous solid" rather than "amorphous compound." *Id*. (citing Jorjani Decl., Ex. 1 (Myerson Dep.) at 139-140 (conceding that references in Exhibits 10 and 11 "support the understanding of what an amorphous solid is")). Further, Defendants contend, "none of Dr. Myerson's cited references dispute[s] the plain meaning of 'amorphous compound.'" *Id*.

With respect to the intrinsic evidence, Defendants, like Takeda, point to the use of the term "amorphous substance" in Reference Examples 1 and 2 of the '282 specification. *Id*. That term, Defendants assert, like the term "amorphous compound," would have been understood by a person skilled in the art to include solids and non-solids, such as oils and liquids. *Id*. (citing Rogers Decl., ¶ 28; Jorjani Decl., Ex. 1 (Myerson Dep.) at 137).

Defendants reject Takeda's assertion that Reference Examples 1 and 2 indicates that the term "amorphous compound" must refer to a solid. *Id*. Defendants point out that these reference examples do not specify the physical state of the amorphous substances described in them. *Id*. at 20-

21. Defendants further assert that the words "evaporat[ing] to dryness" in these reference examples do not support Takeda's position because it was understood in the art that evaporating or drying a substance did not necessarily result in a solid compound, especially in the case of dexlansaprozole. *Id*. at 20-21. In support of this contention, Defendants offer three references that they contend illustrate that drying or evaporating can give rise not only to a solid but also to a liquid or oil. *Id*. (citing Jorjani Decl., Ex. 4 (U.S. Pat. No. 4,191,830 ("the '830 patent") at Example 49, col. 46, ll. 33-51 ("The ether solution is evaporated in vacuo to afford 52.85 grams of a colorless liquid"); *id*., Ex. 5 (U.S. Pat. No. 5,128,356 ("the '356 patent") at Reference Example 25, col. 25, ll. 12-32) ("The solvent was evaporated to dryness to give an oily residue"); *Id*., Ex. 6 (WO 97/02261 ("Von Unge") at Example 12, col. 16, ll. 1-10 ("[e]vaporation of the filtrate afforded an oil with enhanced optical purity")). As to Von Unge, Defendants point out that in prosecuting the '276 patent (a parent patent to the '282 patent), Takeda relied on Example 12 to show that obtaining a *crystal* form of dexlansoprazole was "not a trivial matter." *Id*. at 21 (citing Rogers Decl., Ex. 6 at DEX0001948). Defendants note that in Von Unge, as in Reference Examples 1 and 2 of the '282 patent, the process described involves evaporating solvent from a filtrate. *Id*. at 21.

Defendants also reject Dr. Myerson's additional reason for concluding that the words "amorphous substance" in Reference Examples 1 and 2 must refer to a solid, namely, that Reference Example 2 compares a solid crystalline form with an "amorphous substance" and a person skilled in the art would have understood that the comparison was of "like to like." *Id*. (citing Myerson Decl. ¶ 84). Defendants again point to the prosecution history of the '276 patent, in which the patentees argued that Reference Example 2 afforded "surprising results" because when a crystalline enantiomer was compared with "its corresponding amorphous form," the former was significantly more stable. *Id*. at 21 (citing Rogers Decl., Ex. 6 at DEX0001948-0001949). The patentees went on to cite a prior art reference in which the author compared the stability of the solid form of the compound with the same compound dissolved in a solution. *See* Rogers Decl., Ex. 6 at DEX0001948-0001949 (citing Sukenik, et al., J. Am. Chem. Soc. (1975) vol. 97, no. 18, pp. 5290-5291 (hereinafter, "Sukenik")). In particular, the patentees stated that Sukenik "provides an example wherein a benzenesulfonate is indefinitely stable in solution (amorphous form), but is much less

stable as a solid." Defendants argue that the patentees' comparison of the stability of a crystalline material to that of an amorphous material that was clearly in liquid form (to the extent the compound was dissolved in a solution) shows that Dr. Myerson is incorrect in his assertion that a person skilled in the art would not compare a solid to a non-solid for the purpose of evaluating stability. *Id*

In its Reply Claim Construction Brief, Takeda argues that "while it is true that liquids and gases are 'amorphous,' when used as a modifier, the term 'amorphous' typically describes non-crystalline *solids*." Takeda Reply Claim Construction Brief at 7 (emphasis in original). In support of this point, Takeda cites to two references that it also cited in its Opening Claim Construction Brief, the Hancock and Zografi and the Hsien-Hsin Tung references. *Id*. (citing Myerson Decl., Exs. 10, 14). As to the latter reference, Takeda concedes that it was published in 2009, after the 1999 priority date, but notes that Defendants' expert, Dr. Rogers, testified at his deposition that the terms "amorphous compound" and "amorphous substance" have not changed between 1999 and the present. *Id*. n. 7 (citing Cox Decl., Ex. 10 (Rogers Dep.) at 16-17).

In addition, Takeda cites several references that it did not cite in its Opening Claim Construction Brief. *Id*. First, it cites a 1999 science and technology encyclopedia that contains the following definition of the term "amorphous substance":

> Non-crystalline solid; its atoms or molecules have no regular order. Supercooled liquids such as glass, rubber, and some plastics are amorphous. Many powders appear amorphous but are microcrystalline in structure.

Id. (citing Cox Decl., Ex. 7 (Rogers Dep. Ex. 35, Science and Technology Encyclopedia (University of Chicago Press) (1999) at 17). Second, it cites a 1993 chemistry dictionary that defines "amorphous" as follows:

> a term applied to solids in which the constituent particles (atoms, ions or molecules) do not display periodic long-range order. . . . [Amorphous] substances correspond in their structure to liquids, but differ from them because the particles are not mobile. They are sometimes called *supercooled liquids* in which the friction between particles is very great. . . Glasses are among the most important [amorphous]. Occasionally gases and liquids are called [amorphous] due to their lack of long-range order.

Id. (citing Cox Decl., Ex. 8 (Rogers Dep. Ex. 36, Concise Encyclopedia: Chemistry (Hans-Dieter Jakubke, Hans Jeschkeit, eds., Walter de Gruyter & Co.)(1993)) (emphasis in original)). Third, Takeda cites a 1990 article in which the authors distinguish between the "amorphous state" and the

"highly viscous oily state." *Id*. (citing Cox Decl., Ex. 9 (Rogers Dep. Ex. 27, E.A. Prodan, "State of matter and its reactivity," Reactivity and Solids (1990) vol. 8 at 309)).

Finally, Takeda points to the '668 patent, which it contends is important because it is a pharmaceutical patent, even if it is not in the same patent family as the '282 patent. *Id*. at 7-8. According to Takeda, in the '668 patent the word "amorphous" is used to refer to solids, and *not* to oils. *Id*. (citing '668 patent, col. 5, ll. 1-4) ("The (R)-lansoprazole or (S)-lansoprazole produced by the above-mentioned method may be a solid (crystal, amorphous) or an oily substance").

Takeda argues that in determining the meaning of "amorphous compound," as that term is used in the claims of the '282 patent, the context in which the term is used is particularly important. *Id*. at 8. Takeda points out that Dr. Rogers conceded in his deposition that skilled artisans sometimes use the terms "amorphous state," "amorphous substance" and "amorphous compound" to refer specifically to solids and that "people can use the term differently under different contexts." *Id*. (citing Cox Decl., Ex. 10 (Rogers Dep.) at 31-33, 38, 51-52, 59-62). Takeda argues that because the term "amorphous compound" is used in the context of a pharmaceutical patent, references from that field are more relevant to the meaning of the claim term than references from the general field of chemistry. *Id*. (citing *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998)). Takeda further asserts that Defendants' position should be rejected because Defendants have cited references from the field of chemistry generally, whereas Takeda has cited references from the pharmaceutical field. *Id*. at 8.

In addition, Takeda argues, a person skilled in the art would have understood that "amorphous compound" referred to a solid in the context of the '282 patent because the specification of that patent contains extensive discussion of crystalline compositions of dexlansoprazole. *Id*. (citing Cox Decl., Ex. 10 (Rogers Dep.) at 12, 15 ("[t]he '282 patent is directed to the synthesis, the stereo resolution, and the crystallization of a pharmaceutical")). Because a crystal is known to be a solid, Takeda contends, a person skilled in the art would understand that "the amorphous counterpart to a crystalline solid pharmaceutical composition would itself be a solid." *Id*.

Takeda also points to an FDA guidance entitled "Pharmaceutical Solid Polymorphism" in support of its proposed construction. *Id*. at 8 (citing Cox Decl., Ex. 11 (Rogers Dep. Ex. 33)

(hereinafter "FDA Guidance")). That reference states that drugs can come in various "polymorphic forms," which are defined as crystalline forms, amorphous forms, and solvates. *Id*. At his deposition, Dr. Rogers testified that in the context of this article, he understood the term "amorphous form" to refer to a solid. *Id*. (citing Cox Dec., Ex. 10 (Rogers Dep.) at 64-65). According to Takeda, Dr. Rogers' testimony supports its position that in the pharmaceutical context, an "amorphous compound" is understood to be a solid. *Id*. Takeda also cites to another reference that comes from the pharmaceutical literature that it contends supports its proposed construction. *Id*. (citing Cox Decl., Ex. 12 (Rogers Dep. Ex. 31) (Stephen Byrn, et al., "Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations," Pharmaceutical Research, Vol. 12, no. 7 (1995) (hereinafter "Byrn") at 952 (stating that "there are cases where the amorphous forms is [sic] the only solid form that has adequate bioavailability")). *Id*. Takeda notes that at his deposition, Dr. Rogers was unable to name any orally ingested pharmaceutical product that used an oil or a gas, even though these forms fall within Defendants' proposed definition of "amorphous compound." *Id*. (citing Cox Decl., Ex. 10 (Rogers Dep.) at 58-59, 72).

Takeda rejects Defendants' reliance on the statements made during prosecution of the '276 patent regarding Reference Examples 1 and 2. *Id*. at 9 n. 8. Takeda argues that these statements "were made with regard to the term 'amorphous compound,' a term which does not appear in the '276 patent." *Id*. Further, Takeda argues, these statements have nothing to do with the "amorphous substance" described in the '282 patent because they were "part of a broader explanation of why the prior art Larsson reference, which explicitly discloses isolating dexlansaprazole in liquid form as an oil, did not render the crystals of the '276 patent obvious." *Id*. (citing Rogers Decl., Ex. 6 (excerpt of '276 patent prosecution history) at DEX0001946-49).

Takeda also argues that Defendants' proposed construction should be rejected because it would ensnare prior art that was before the PTO when it considered the application that resulted in the issued '282 patent, namely Von Unge and Larsson.[10] *Id*. at 9 (citing *Apple Comp., Inc. v.*

[10]In its brief, Takeda mistakenly referred to WO 97/2261 as "Larsson." Reply at 9. At oral argument, Takeda made clear that it advances this argument as to both Larsson (WO 96/02535) and Von Unge (WO 97/02261).

Articulate Sys., Inc., 234 F.3d 14, 24 (Fed. Cir. 2002)); *see also* '282 patent (listing both Von Unge and Larsson under the heading "References Cited")). Takeda points out that in the Reasons for Allowance issued by the PTO in connection with the '058 patent (a parent patent of the '282 patent), the examiner expressly recognized that Larsson and Von Unge taught the oily R stereoisomer. *Id*. (citing Cox Decl., Ex. 13). Indeed, at oral argument, Takeda offered a page from the patent prosecution history of the '058 patent with a handwritten note in connection with the Larsson reference stating "oil obtained not solid at all." Claim Construction Hearing, February 16, 2012, Takeda Slide 83.

2. Analysis

The term "amorphous compound" is used in the claims of the '282 patent but is not used in the specification, much less defined. Therefore, the Court begins its analysis by looking to the extrinsic evidence for guidance on the generally accepted meaning of the term "amorphous compound" in the field of the invention.

As a preliminary matter, the Court addresses the relevant field of the invention, and in particular, Takeda's assertion in its Reply brief that references from the "broader field of chemistry" (as opposed to the narrower field of pharmaceutical science) are of "marginal relevance to understanding the meaning of the claim term [amorphous compound]." *See* Takeda's Reply Brief on Claim Construction at 8. It is undisputed that the '282 patent is directed at a pharmaceutical. *See* Cox Decl., Ex. 10 (Rogers Dep.) at 12, 15 ("[t]he '282 patent is directed to the synthesis, the stereo resolution, and the crystallization of a pharmaceutical"); Myerson Decl. ¶ 50 (listing qualifications of a person skilled in the art, including experience in the pharmaceutical industry related to, *inter alia*, crystallization or detection and/or evaluation of solid state forms"). This does not mean, however, that references from the general field of chemistry may not be helpful for developing an understanding of how this term is used in the '282 patent. Indeed, Takeda relied on a number of references taken from the general field of chemistry in support of its proposed construction. *See, e.g.,* Cox Decl., Ex. 7 (definition of "amorphous substance" taken an encyclopedia of science and technology), Ex. 8 (definition of "amorphous" from a chemistry encyclopedia). Therefore, while the Court finds the references from the pharmaceutical field to be particularly helpful, as discussed

further below, it does not limit its consideration of the extrinsic evidence to references that are specifically related to pharmaceuticals.

Looking to the various definitions offered by the parties, the Court concludes that there is more than one possible meaning of the word "amorphous" as used by a person skilled in the art in the field of chemistry. In particular, while some definitions of "amorphous" or terms that use the word "amorphous" appear to include liquids and gases, *see, e.g.,* Rogers Decl., Ex. 4 (Hawley's Condensed Chemical Dictionary) at 75 ("all liquids are amorphous"); Myerson Decl., Ex. 15 (McGraw-Hill Concise Encyclopedia of Science and Technology) at 84-85 ("A solid is distinguished from its other amorphous counterparts (liquids and gases) by its viscosity"), others limit the definition of these terms to a solid. *See, e.g.,* Cox Decl., Ex. 7 (Science and Technology Encyclopedia at 17, defining "amorphous substance" as "[n]on-crystalline solid"). These alternate meanings are expressly recognized in some of the definitions offered by the parties. For example, in an 1993 encyclopedia of chemistry, it is stated that "amorphous" is "a term applied to solids" but that "[o]ccasionally gases and liquids are called [amorphous] due to their lack of long-range order." Cox Decl., Ex. 8 (Concise Encyclopedia: Chemistry) at 67). Similarly, the "Ulicky" reference cited by Defendants and also listed among the references before the PTO on the '668 patent recognizes that there is "ambiguity" as to the definition of "amorphous substance."

In light of these alternate meanings, the Court rejects Defendants' assertion that Takeda is required to show that it clearly disavowed a construction of "amorphous compound" that includes gases and liquids. That rule applies only when an inventor "deviate[s] from the ordinary and accustomed meaning of a claim term." *Epistar*, 566 F.3d at 1334. Here, there appear to be two possible meanings of the term, *both* of which might be characterized as the "ordinary and accustomed meaning" of the claim term. Thus, the general standard set forth in *Phillips* and *Vitronics*, discussed above, applies.

With this standard in mind, the Court looks to the intrinsic evidence to determine which of these possible definitions is consistent with the use of the claim term "amorphous compound" in the '282 patent. First, the Court addresses the significance of Reference Examples 1 and 2 of the '282 patent. The parties vigorously dispute the significance of these examples. Takeda argues that a

person of ordinary skill in the art would have understood that the "amorphous substance" that is described in them is a solid, and *not* a liquid or gas, while Defendants contend the term encompasses all three forms. Although a close call, the Court finds Takeda's position to be more persuasive.

In Reference Examples 1 and 2, the patentees expressly state that the amorphous substance is obtained using a process that involves "evaporat[ing] to dryness" isolated dexlansoprazole. '282 patent, col. 8, ll. 3-6, 25-29. Dr. Myerson has opined that this language would have indicated to a person skilled in the art that the amorphous substance was a solid. Myerson Decl. ¶ 83. In support of this opinion, Dr. Myerson explained at his deposition that "if somebody produces an oil in an example, they say an oil. If they produce an amorphous solid, they would normally say an . . . amorphous substance." Jorjani Decl., Ex. 1 (Myerson Dep.) at 164. Dr. Myerson further testified that "amorphous substance" and "amorphous compound" would be understood to mean the "identical thing." *Id*. at 142. The references cited by Defendants to show that evaporation can yield an oil are, in fact, consistent with Dr. Myerson's opinion. In particular, all of them call out the fact that the processes that are being described give rise to a liquid or oil. *See* Jorjani Decl., Ex. 4 ('830 patent) at Example 49, col. 46, ll. 33-51 ("The ether solution is evaporated . . .to afford . . . a colorless liquid"); *id*., Ex. 5 ('356 patent) at Reference Example 25, col. 25, ll. 12-32) ("The solvent was evaporated to dryness to give an oily residue"); *Id*., Ex. 6 (Von Unge) at Example 12, col. 16, ll. 1-10 ("[e]vaporation of the filtrate afforded an oil ")). The failure of the patentees to state that the amorphous substance obtained in Reference Examples 1 and 2 by way of evaporation was a liquid or oil supports the conclusion that these examples referred to *solids* when they used the term "amorphous substance."

The arguments made by the patentees in connection with the '276 patent application do not support a contrary conclusion, although they do suggest that Takeda's alternative argument – that a person skilled in the art would understand that in Reference Example 2, the amorphous substance must be a solid because it is being compared to a crystalline material – is incorrect. In the prosecution history, the patentees offered Sukenik to support the thesis that "a crystalline material will be more stable than its corresponding amorphous form." Rogers Decl., Ex. 6 at DEX0001949. Sukenik, in turn, addressed the stability of a benzenesulfonate "in solution (amorphous form)" as

compared to the stability of benzenesulfonate in solid form. *Id*. The comparison of the stability of a liquid to a solid to show that "a crystalline material will be more stable than its corresponding amorphous form" directly contradicts Dr. Myerson's contention that a person skilled in the art would have understood that Reference Example 2 described the comparison of like to like, that is, a solid to a solid.[11] The usage of the word "amorphous" in the patentee's submission to the PTO, however, is entirely consistent with Dr. Myerson's opinion that when an amorphous substance is something *other* than a solid, that is, a liquid or gas, it is expressly identified as such. In particular, the patentees make clear that the amorphous form at issue in Sukenik is a liquid.

Takeda's assertion that in the context of the pharmaceutical field, reference to an "amorphous substance" or "amorphous compound" means a solid unless otherwise stated appears to be consistent with the pharmaceutical references offered by the parties. In particular, the vast majority of the pharmaceutical references offered, including the '668 patent, the FDA Guidance, Hancock and Zografi, Hsien-Hsin Tung, and Byrn, involved amorphous compounds that are solids. These references indicate that typically, at least, amorphous materials used in oral pharmaceuticals are solids. It was for this reason, perhaps, that Dr. Rogers was hard-put at his deposition to name any orally ingested non-solid amorphous material used in pharmaceuticals, though he testified that they exist.

Finally, the Court turns to Takeda's argument that the term "amorphous compound" should be construed so as to avoid ensnaring prior art, namely, Larrson and Von Unge. As Defendants pointed out at oral argument, the rule that claims should be construed to preserve their validity is a principle that has not been applied broadly. Rather, the Federal Circuit has cautioned against "judicial rewriting of claims to preserve validity." *Liebel-Flarsheim Co. v. Medrad, Inc*., 358 F.3d 898, 911 (Fed. Cir. 2004)(quoting *Rhine v. Casio, Inc.*, 183 F.3d 1342, 1345 (Fed.Cir.1999)). In *Liebel-Flarsheim*, the court held that "unless the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous, the axiom regarding the construction to

[11]For the same reason, the Court finds unpersuasive Takeda's more general argument that because the '282 patent addresses crystalline materials, a person skilled in the art would understand that the claimed "amorphous compound" must be the counterpart to the crystalline material and therefore also a solid.

preserve the validity of the claim does not apply." It is not clear to the Court that this is such a case, given that there is both intrinsic and extrinsic evidence to suggest that the patentees used the term "amorphous compound" to refer to a solid, as appears to have been the more common usage in the pharmaceutical literature. Assuming the term remains ambiguous, however, this rule also supports Takeda's position.

The prior art at issue – Von Unge and Larsson – was before the PTO when it considered the application that led to the issuance of the '282 patent. Further, the prosecution history of the '058 patent, which is a parent patent, indicates that the examiner was aware that Von Unge and Larsson related to oils. *See* Cox Decl., Ex. 13 (Reasons for Allowance). Similarly, the arguments made by the patentee's in support of the '276 patent application that were cited by Defendants state that Von Unge involved the isolation of an oil rather than a solid. *See* Rogers Decl., Ex. 6 at DEX0001948. Under these circumstances, Defendants' proposed construction would run counter to the rule that the Patent Office is presumed to have properly done its job. *See Tokai Corp. v. Easton Enterprises, Inc.*, 632 F.3d 1358, 1367 (Fed. Cir. 2011). Thus, to the extent the claim term "amorphous compound" is ambiguous, the term should not be construed to encompass liquids and gases.

The Court adopts Takeda's proposed construction of the term "amorphous compound."

G. "released in the pH range of no less than 5.0 to no more than 6.0" ('755 patent, claim 1)/"soluble in the pH range of 6.0 to 7.5" ('755 patent, claim 1)/ "soluble in the pH range of no less than 6.5 to no more than 7.0" ('755 patent, claim 7)

Claim Term	Proposed Constructions
"released in the pH range of no less than 5.0 to no more than 6.0" [hereinafter, the "release limitation"]	**Takeda**: "begins to be released from the tablet, granule, or fine granule into the body at pH values within the range from 5.0 to 6.0" **TWi**: Phrase is indefinite **Impax and Handa**: Plain meaning

"soluble in the pH range of 6.0 to 7.5"	**Takeda**: "begins to dissolve in the gastrointestinal tract at pH values within the range from 6.0 to 7.5" **TWi**: Phrase is indefinite **Impax and Handa**: Plain meaning
"soluble in the pH range of no less than 6.5 to no more than 7.0" [hereinafter, this term and the preceding term are referred to together as "the solubility limitations"]	**Takeda**: "begins to dissolve in the gastrointestinal tract at pH values within the range from 6.0 to 7.5." **TWi**: Phrase is indefinite **Impax and Handa**: Plain meaning

The '755 patent is directed to controlled-release formulations containing, *inter alia*, dexlansoprazole. The claims-in-suit are specifically directed to a composition that employs a dual-delayed release mechanism that uses two different types of enteric coatings.[12] In particular, Independent claim 1, and dependent claim 7, read as follows:

> 1. A capsule comprising:
>
> composition (i) comprising a tablet, granule or fine granule in which a release of an active ingredient is controlled; said tablet, granule or fine granule comprising a core particle containing an imidazole compound. . . and
>
> a pH-dependently soluble release-controlled coating-layer which comprises one kind of polymeric substance or a mixture of two or more kinds of polymeric substances having different release properties selected from [generic categories of polymeric substances]; **said polymeric substance is soluble in the pH range of 6.0 to 7.5**, and

[12]Takeda's expert, Dr. Charman, offers the following background information relating to enteric coatings:

> An enteric coating protects the drug core from disintegration in the acidic environment of the stomach. Polymers such as hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, and polyvinyl acetate phthalate are commonly used as enteric coatings in pharmaceutical products. These enteric coating materials are designed to dissolve (and hence release drug) once the pH of the local environment exceeds a particular pH value. Typically, they will not dissolve within the acidic environment of the stomach but they will then rapidly dissolve in a pH-dependent manner at the pH values encountered within the small and large intestine.

Declaration of William M. Charman, Ph.D., in Support of Takeda's Opening Claim Construction Brief ("Charman Decl.") ¶ 38.

composition (ii) comprising a tablet, granule or fine granule comprising a core particle containing the active ingredient and enteric coat such that **the active ingredient is released in the pH range of no less than 5.0 to no more than 6.0**.

7. The capsule according to claim 1, wherein the pH-dependently soluble release-controlled coating-layer of the tablet, granule or fine granule in which the release of the active ingredient is controlled is a layer **soluble in the pH range of no less than 6.5 to no more than 7.0.**

'755 patent, claims 1, 7 (disputed claim terms in bold). The primary disputes relate to: 1) whether the pH ranges specified in these claim terms refer to when release of the active ingredient, or dissolution of the enteric coating, begins, as Takeda contends, or rather, represent the *only* pH values at which release or dissolution occurs; and 2) whether the dissolution and release referred to in the claims occurs in the body.

Takeda argues that its proposed constructions are consistent with, and supported by, the surrounding language of the claims and the patent specification. Takeda Opening Claim Construction Brief at 21-22 (citing Charman Decl. ¶¶ 58-86). It points to the limitation that precedes the claim terms at issue, describing the coating layer for the granule of composition (i) as a "pH dependently soluble release-controlled layer which comprises one kind of polymeric substance or a mixture of two or more kinds of polymeric substances having different release properties." *Id*. According to Takeda, this limitation supports the conclusion that the ranges set forth in claims 1 and 7 reflect the pH values at which the coating layer *begins* to dissolve. *Id*. at 21-22. Takeda points out that Impax and Handa's proposed construction of this claim limitation is consistent with its position. *Id*. at 22 (citing Joint Claim Construction and Prehearing Statement [Docket No. 52], App'x B, at 28 (stating that this limitation should be construed to mean "a coating layer that delays or extends the release of active ingredient by dissolving or releasing drug, and/or allowing diffusion of drug, said coating layer comprising one kind of polymeric substance or a mixture of two or more kinds of polymeric substances, each of which begins to dissolve at a different pH value")).

Takeda argues further that its proposed constructions are supported by the '755 specification, which repeatedly defines the phrase "pH dependently soluble" to mean "releasing an active ingredient under the circumstances of more than a certain pH value." *Id*. at 22 (citing '755 patent, col. 142, ll. 62 - 64; col. 143, ll. 27 - 29; col. 145, ll. 16 - 18; col. 145, ll. 50 - 52; col. 147, ll. 2 - 4;

col. 147, ll. 34 - 36; col. 152, ll. 27 - 28; col. 152, ll. 62 - 63; col. 154, ll. 2 - 4; col. 154, ll. 33 - 35; col. 156, ll. 33 - 34; col. 159, ll. 60 - 61). Takeda also points to the statement in the specification that "'pH-dependently' means that the coating material is dissolved/eluted under the circumstances of more than a certain pH value to release an active ingredient." *Id*. (quoting '755 patent, col.9, ll.32-35). According to Takeda, this language supports the conclusion that the polymeric enteric coatings referred to in the specification have a threshold pH at and above which they will dissolve and release the active ingredient. *Id*. Another statement in the specification that Takeda asserts supports this conclusion is the following:

> It is desirable that the coating material is used alone or, if necessary, in combination so that the polymer is dissolved preferably at a pH of 6.0 or above, more preferably at a pH of 6.5 or above, and further more preferably at a pH of 6.75 or above. Further, more desirably, a polymer soluble at a pH of 6.0 or above and a polymer soluble at a pH of 7.0 or above are used in combination, and furthermore desirably, a polymer soluble at a pH of 6.0 or above and a polymer soluble at a pH of 7.0 or above are used in combination at a ratio of 1:0.5 to 1:5.

Id. (citing '755 patent, col.9, l.65 to col.10, l.7). Thus, the specification makes clear, Takeda contends, that when the claims refer to dissolution or release occurring "in the pH range of no less than 5.0 to no more than 6.0," "in the pH range of 6.0 to 7.5," or "in the pH range of no less than 6.5 to no more than 7.0," it is providing a range of pH values within which dissolution or release begins, rather than a range imposing both a lower and an upper limit on when dissolution or release occurs. *Id*. at 22-23 (citing Charman Decl. ¶¶ 65-66).

Takeda further cites to the knowledge of a person skilled in the art about the commercially available polymers that can be used to achieve the dissolution and release properties set forth in the claims. *Id*. at 23. As an example, Takeda points to the methacrylic acid polymers listed in claim 1, and to the specific examples of such polymers in the '755 specification, including: Eudragit L30D-55 (methacrylic acid-ethyl acrylate copolymer), Eudragit L100 (methyl methacrylate-methacrylic acid copolymer), and Eudragit S100 (also a methyl methacrylate-methacrylic acid copolymer). *Id*. (citing '755 patent, col.9, ll.46-55). According to Takeda, the Eudragit polymers

are manufactured by Evonik Industries.[13] *Id*. Evonik Industries, in turn, states in its marketing materials that the enteric coatings referenced in the '755 specification exhibit dissolution "above pH 5.5" for Eudragit L30D-55, "above pH 6.0" for Eudragit L100, and "above pH 7.0" for Eudragit S100. *Id*. (citing Charman Decl., Ex. 6 at DEX0014573, Ex. 7 at DEX0014559).

Similarly, Takeda points to the polymer hydroxypropylmethyl cellulose phthalate in claim 1, and the examples of suitable brands of such a polymer set forth in the specification, including HP-50 and HP-55, manufactured by Shin-Etsu Chemical Co., Ltd. *Id*. at 24 (citing '755 patent, col. 9, ll. 42 - 45). Shin-Etsu Chemical Co., Ltd., in turn, states in its brochure that these polymers are soluble at pH values greater than or equal to 5.0 or 5.5, respectively. *Id*. (citing Charman Decl., Ex. 8 (ShinEtsu Chemical Co., HPMCP: Enteric Coating Material (Sept. 2009)) at DEX0014692). According to Takeda, each of the polymers listed in the specification as suitable for use as the pH-dependent release-control layer will begin to dissolve at a particular threshold pH, but also dissolve at higher pHs. *Id.* (citing Charman Decl. ¶¶ 60-63, 75-77, 82-84). Further, Takeda contends, none of the exemplary polymers listed in the specification is soluble only in the pH range of pH 5.0 to 6.0, or in the pH range of pH 6.5 to 7.0. *Id.*

Finally, Takeda argues that it is clear that the dissolution and release referred to in the claims occurs in the gastrointestinal tract. *Id*. (citing Charman Decl. ¶¶ 67-72, 78, 85). According to Takeda, this is because the specification discusses the inventive formulation's behavior within the gastrointestinal tract. *Id*. In particular, the specification notes that "a composition containing a benzimidazole compound having a proton pump inhibitor action is needed to disintegrate rapidly *in the small intestine*." *Id* (citing '755 patent, col. 1, ll. 45 - 50 (emphasis added by Takeda)). Takeda also points to the statement that "the coating material of the present invention is preferably a substance which is dissolved at a higher pH, . . . and controls more favorably the release of drug *in the stomach*." *Id*. (citing '755 patent, col. 9, ll. 36-41 (emphasis added by Takeda)). In addition, Takeda notes that a basic goal of the dual enteric-coating method described and claimed in the patent

[13]The '755 specification states that these polymers are manufactured by Rohm Co. '755 patent, col. 9, l. 50. Dr. Charman explains that Rohm Co. is now known as Evonik Industries. Charman Decl., ¶ 62 n. 3.

is to provide for two separate releases of drug occurring at different parts of the gastrointestinal tract, and thus at different times. *Id*. (citing '755 patent, col. 6, ll. 43 - 45 (noting that "the persistence of blood levels after oral administration is remarkably prolonged by these combinations [of coatings]"); Charman Decl. ¶ 68).

Takeda contends that its position finds further support in the product literature of the companies that manufacture these polymers, such as Evonik, which describe their products in terms of how they are released within the human body. *Id*. at 24-25. For example, Evonik describes the polymers referenced in the '755 specification as providing "drug delivery in the duodenum" (Eudragit L30 D-55), "drug delivery in jejunum" (Eudragit L100) and "colon delivery" (Eudragit S 100). *Id*. at 25 (citing Charman Decl., Ex. 7 at DEX0014568-69). Takeda also points to a diagram of the digestive system showing where in the gastrointestinal tract the methacrylic acid polymers in claim 1 of the '755 patent are dissolved. *Id*. (citing Charman Decl, Ex. 7 at DEX0014571). Finally, Takeda points to Evonik product literature stating that "the different grades can be combined with each other, making it possible to adjust the dissolution pH, and thus to achieve the required GI targeting for the drug"). *Id*. (citing Charman Decl., Ex. 6 at DEX0014573).

Defendants Handa and Impax argue that the disputed pH range terms should be given their plain and ordinary meaning. As to the term "soluble in the pH range of 6.0 to 7.5," Handa and Impax assert this term simply means that solubility must exist within the specified pH ranges but that the term does not restrict solubility outside of that range. Defendants' Claim Construction Brief at 23. On the other hand, Handa and Impax assert, the terms "released in the pH range of no less than 5.0 to no more than 6.0" and "soluble in the pH range of no less than 6.5 to no more than 7.0," should be construed to mean that release/solubility occurs at "no less than" the claimed lower pH value and "no more than" the claimed upper pH value, such that release and solubility do *not* occur outside the specified ranges. *Id*.

According to Handa and Impax, Takeda's proposed constructions is incorrect for several reasons. First, they contend, Takeda ignores the plain meaning of the claim language by eliminating the "no less than/no more than" claim language as to the claim terms that include those words. *Id*. at 23-24. Handa and Impax argue that in doing so, Takeda has failed to adhere to the rule that all the

words of a claim should be given meaning. *Id*. (citing *Pause Tech. LLC v. Tivo, Inc.*, 419 F.3d 1326, 1334 (Fed. Cir. 2005) (a claim construction that gives meaning to all of the words of the claim is preferred over one that does not)).

Second, Handa and Impax assert that Takeda's proposed constructions should be rejected because Takeda has given the claim term that does not include the "no less/no more" language the same meaning as the terms that do include this language. *Id*. In doing so, they argue, Takeda fails to adhere to the rule that different words in the claims are presumed to have different meanings. *Id*. (citing *Applied Med. Res. Corp. v. U.S. Surgical Corp*., 448 F.3d 1324, 1333 n. 3 (Fed. Cir. 2006) ("[T]he use of . . . different terms in the claims connotes different meanings")).

Handa and Impax also reject Takeda's reliance on the brochures and marketing materials for the commercially available polymers referenced in the '755 specification, arguing that Takeda is attempting to redraft claims to sustain their validity. *Id*. (citing *Chef America, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1374 (Fed. Cir. 2004)).

Handa and Impax further contend that Takeda's proposed constructions are incorrect because Takeda is attempting to import a limitation – specifically, "begins to be released" and "begins to be dissolved" – from the specification. *Id*. at 24- 25. According to Handa and Impax, the written description cannot be used to substitute for or redraft the claim language. *Id*. at 25 (citing *Resonate Inc. v. Alteon Websystems, Inc.*, 338 F.3d 1360, 1364 (Fed. Cir. 2003)).

Handa and Impax reject Takeda's reliance on the phrase in claim 1 claiming a "pH-dependently soluble release-controlled coating-layer which comprises one kind of polymeric substance or a mixture of two or more kinds of polymeric substances having different release properties." *Id*. According to Handa and Impax, "[t]his phrase . . .does not share the same distinctive language found in the pH range limitations and is thus not instructive for construing them." *Id*. Furthermore, they argue, the phrase relates only to composition (i) of claim 1 and not to composition (ii), which includes the "no more/no less" language. *Id*. Therefore, it is improper to consider this claim language to construe claim terms used to claim composition (ii). *Id*. As to the pH range term appearing in claim 7, Handa and Impax argue that while the term relates to the "pH-dependently soluble release-controlled coating layer" of composition (i), it includes the "no

less than/no more than" language used in the pH range term of composition (ii), and thus mirrors that term. Therefore, they contend, the pH range terms of claim 7 and composition (ii) should be construed consistently. *Id*.

Handa and Impax also argue that in relying on the specification, Takeda has ignored language that conflicts with its argument. *Id*. at 26. In particular, Handa and Impax quote language in the specification describing "a core particle containing an active ingredient and enteric coat which is dissolved, thereby an active ingredient being released in the pH range of no less than 5.0, nor more than 6.0." *Id*. (citing '755 patent, col. 5, l. 66 - col. 6, l. 2). According to Handa and Impax, this disclosure supports their plain meaning constructions because it indicates that the process of releasing the active ingredient must be *completed* within the stated range. *Id*.

Handa and Impax also challenge Takeda's assertion that these terms should be construed to include the limitations "in the body" and "in the gastrointestinal tract." *Id*. Handa and Impax point to the statement in the specification stating as follows:

> [T]he pH mentioned here means a pH of the McIlvaine solution or Clark-Lubs solution. Hereinafter, the pH of a pH-dependently soluble layer means the pH of these solutions.

Id. (citing '755 patent, col. 7, ll. 2-5). According to Handa and Impax, neither McIlvaine nor Clark-Lubs solutions exists in the body, and there is no example or mention of any in-body pH testing in the '755 patent. *Id*. (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 69:15-70:7 (testifying that McIlvaine solution is used as a "surrogate for what occurs in the gastrointestinal tract")). Handa and Impax also point to the prosecution of the '755 patent, noting that Takeda submitted a declaration in support of the application describing dissolution testing of the '755 claimed subject matter. *Id*. at 26 (citing Jorjani Decl., Ex. 3 ('755 patent file history excerpt at DEX7123-24, 7130-33)). That testing, they contend, was not conducted in the body, but rather occurred in a phosphate buffer outside the body. *Id*.

TWi argues that all of the pH range claim terms are indefinite. *Id*. at 27. First, addressing the term "active ingredient is released in the pH range of no less than 5.0 to no more than 6.0," TWi argues that "a skilled artisan could not cull from the claims, specification and prosecution history any objective standard (i.e. test conditions) to determine whether the active ingredient is released

within the specified pH range." *Id*. In particular, TWi asserts that although the range is described to the one-tenth of a pH value, and although the parties appear to agree that the pH range would be determined using "some kind of dissolution," key information is missing regarding how to make this determination. *Id*. at 27-28 (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 124:18-127:16 (testifying that pH would be measured at least to one decimal point); '755 patent at col. 7, ll. 2-5 (referring to pH of the McIlvaine solution or Clark-Lubs solution); Jorjani Decl., Ex. 2 (Charman Dep.) at 70: 1-18, 111: 5-13, 237: 10-20 (testifying that a variety of tests could be used to determine pH); Expert Declaration of Thomas L. Reiland, Ph.D. In Support of Defendants Anchen Pharmaceuticals, Inc.'s and TWi Pharmaceuticals, Inc.'s Opening Claim Construction Brief ("Reiland Decl."), ¶¶ 20-22 (stating that claim term is indefinite because although it refers to dissolution testing, no basis is provided for determining dissolution test criteria)).

According to TWi, Takeda's expert admitted that "[d]issolution studies are typically defined by a certain volume, a temperature, and different components," and that there are "a whole range of different materials – solvents, salts, pHs – that can be used for dissolution studies." *Id*. (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 77:3-11). Thus, a skilled artisan would not know what dissolution test to use to determine whether the claim element is met and is left to guess as to the terms' metes and bounds. *Id*. (citing Reiland Decl., ¶¶ 23-27, 32). Even Takeda's expert could not state what test should be used to determine whether the claim term was met, TWi asserts. *Id*. (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 112:8-113:1). Because the skilled artisan would not be able to determine whether the metric listed in the claim is met, the term is indefinite, TWi contends. *Id*. (citing *Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1340 (Fed. Cir. 2003)).

According to TWi, Takeda's proposed definition of the claim term "further exacerbates the indefiniteness problem" to the extent Takeda seeks to substitute "is released" with "begins to release." *Id*. at 29. TWi points to the testimony of Takeda's expert that it is "impossible" to determine the amount or percentage that would constitute what "begins to release" means and notes that Takeda's counsel objected that the phrase was "vague, ambiguous, incomprehensible, unintelligible and incomplete." *Id.* (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 111:14 - 112:5).

TWi also asserts that Takeda's expert used "released" throughout his declaration to mean "the release of the drug" and not "begins to release. *Id.* (citing Charman Decl., ¶¶ 24, 35, 37).

Further, TWi argues, Takeda's proposed construction is inconsistent with the claim language and the specification. TWi states that when the "specification meant to say begin, it said so." *Id*. at 29. Further, TWi argues, when the specification and prosecution history referred to "is released," "they meant that the active ingredient was (past tense) released." *Id*. (citing '755 patent, col. 1, ll. 34-35 ("a pH-dependent release control of compound and a time-dependent release control wherein the compound is released after a certain lag time"), col. 7, ll. 28-31 ("the release of active ingredient is controlled in the meanwhile, the active ingredient is released continuously or in a pulsatile manner from the tablet"), col. 44, ll. 45-48 ("2 kinds of granules, such as granules wherein the active ingredient is released comparatively quickly and granules wherein the active ingredient is released with prolonged time"); Jorjani Decl., Ex. 3 ('755 patent file history) at DEX0006159 (application claim 41, which corresponds to claim 1 of the issued patent); DEX0006164 ("[b]y having composition (ii) dissolving at pH 5.0-6.0 and (i) that includes the polymeric substance for controlled release at higher pH 6.0-7.5, the capsule formulation of claim 41 releases the active ingredient rapidly from composition (ii) at the pH of the small intestine . . . . Then, the active ingredient that is released from composition (i) later at higher pH 6.0-7.5 maintains the blood level and the efficacy"); DEX0007124 ("[a]t predetermined time periods, an aliquot was withdrawn and the percentage of released Compound A was spectophotometrically determined at 286 nm."); DEX 0007131 ("the plasma level of the active ingredient of claim 41, ie., lansoprazole, released in beagle dogs is maintained in a therapeutically effective level . . . composition (ii) of claim 41 releases the active ingredient in a relatively short period of time"); DEX0007261 (stating in Reasons for Allowance "[t]he instantly claimed compounds are novel and non-obvious over the prior art because of the combination of the two components of the composition, one comprising a compound of formula I' and soluble at pH range 6.0 to 7.5, and the other such that it is released in the pH range of no less than 5.0 to no more than 6.0").

Next, TWi addresses the claim term "said polymeric substance is soluble in the pH range of 6.0 to 7.5" and "a layer soluble in the pH range of no less than 6.5 to no more than 7.0." *Id*. at 29-

30. According to TWi, these terms are indefinite not only because a person skilled in the art would not know what testing methods should be used to determine if the pH range limitations are met, but also because the word "soluble," as used in these claim terms, would not be understood by a person skilled in the art. *Id*. According to TWi, the patentees' use of the term "soluble" in claims 1 and 7 is not consistent with any understood definition of the term soluble because the '755 patent "fails to provide any rubric or method for a skilled artisan to determine whether the polymer or mixtures of polymers listed in the claim 1 Markush group are soluble at a specified pH as contemplated by the claim." *Id*. (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 104:14-107:17)).

Further, TWi contends, the specification uses "soluble" in a manner inconsistent with its accepted meaning. *Id*. at 30. In particular, TWI argues that the '755 specification and Takeda equate "soluble" in the claims to some form of "release." *Id*. An example of such a use, according to TWi, is the statement in the specification that "[h]erein, 'pH-dependently' means that the coating material is dissolved/eluted under the circumstances of more than a certain pH value to release an active ingredient." *Id*. (citing '755 patent at col. 9, ll. 32 - 35). TWi also points to the following statements of the applicants during prosecution relating to application claim 41:

> Composition (i) releases the active ingredient at pH 6.0-7.5, and composition (ii) releases it at pH 5.0-6.0. The two-composition formulation that releases the active ingredient at two different pH is supported by the specification at page 15, line 16 – page 16, line 3.
>
> . . .
>
> Then, the active ingredient that is released from composition (i) later at higher pH 6.0-7.5 maintains the blood level and efficacy.

Id. (citing Jorjani Decl., Ex. 3 ('755 patent file history excerpt) at DEX 0006162, 0006164). According to TWi, "the applicants explained their claims in this manner to address patentability rejections [and] rel[ied] on drug release data to demonstrate that their Dexilant product meets the 'soluble' limitations of claims 1 and 7 of the '755 patent." *Id*. (citing Jorjani Decl., Ex.7 (Plaintiffs' Resp. to TWi Interrog.) at 7; Jorjani Decl., Ex. 2 (Charman Dep.) at 69 -70, 79 - 80).

Finally, TWi asserts that the claim term referencing "a layer" is indefinite, as used in claim 7, because that claim references "a layer" being soluble in a narrower pH range, but the layer of composition (i) is not limited to only soluble materials and may contain insoluble components. *Id*.

Consequently, according to TWi, parts of the "layer" may never become soluble in the restricted pH range. *Id.* (citing Reiland Decl. ¶ 51).

In its Reply brief, Takeda contends that Handa and Impax's plain meaning constructions, under which release and solubility do not occur outside the specified ranges, should be rejected because they would render the claims inoperable and "make[ ] no sense as a matter of basic chemistry." Takeda Reply Brief on Claim Construction at 10. Specifically, Takeda asserts, one skilled in the art would understand that the pH ranges in these claim terms refer to the threshold pH at which an enteric coating will begin to dissolve/release drug because it is well-known that pH-sensitive enteric coatings do not dissolve or release drug only within a particular pH range. *Id*. This is recognized in the specification, Takeda argues, which makes clear that enteric coatings dissolve and release drug at and above particular pH levels. *Id*. (citing '755 patent, col. 9, ll. 32 - 35 ("'pH-dependently' means that the coating material is dissolved/eluted under the circumstances of more than a certain pH value . . . "). According to Takeda, the specification, in discussing the granule that dissolves at the higher of the two pH ranges specified in the claims, repeatedly emphasizes that the pH values are threshold values at and above which dissolution occurs. *Id*. (citing '755 patent, col. 9, l. 65 - col. 10, l. 7).

Takeda further contends that the applicants and the Examiner clearly understood that the claimed ranges referred to threshold values. *Id*. (citing Reiland Decl., Ex. I, at DEX0007130 (noting that composition (ii), the granule in which the active ingredient was "released in the pH range of no less than 5.0 to no more than 6.0," released drug rapidly at pH 6.8)). Indeed, Takeda notes, Dr. Reiland acknowledged that all enteric coatings of which he was aware that are soluble at a pH of 5.5 (the "usual enteric coatings" of the inventive composition) also dissolved at a pH above 6.0, such as 6.5. *Id*. at 11 (citing Cox Decl. Ex. 14 (Reiland Dep.) at 95:23 - 96:10). Takeda further points out that Dr. Reiland, when asked about the polymers listed in claim 1 as suitable for the "layer soluble in the pH range of no less than 6.5 to no more than 7.0" in claim 7, similarly acknowledged that all of those with which he was familiar dissolved at pHs above 7, such as 8.0, and further, that he could not identify any that would not dissolve at a pH higher than 7. *Id*. (citing Cox Decl., Ex. 14 (Reiland Dep.) at 28-29, 31-32, 112-118). Thus, Takeda asserts, under Handa

and Impax's reading, no enteric coating would ever satisfy the pH limitations, rendering the claims completely inoperable – a result that should be viewed with "extreme skepticism." *Id*. (citing *Talbert Fuel Sys. Patents Co. v. Unocal Corp.*, 275 F.3d 1371, 1376 (Fed. Cir. 2002), vacated and remanded on other grounds, 537 U.S. 802 (2002); *AstraZeneca LP v. Apotex, Inc*., 633 F.3d 1042, 1053 n.1 (Fed. Cir. 2010)).

Takeda rejects Handa and Impax's reliance on *Applied Med. Res. Corp. v. U.S. Surgical Corp.*, 448 F.3d 1324 (Fed. Cir. 2006) for the proposition that the phrases "no less than 5.0 to no more than 6.0" and "no less than 6.5 to no more than 7.0," must be construed differently than "in the pH range of 6.0 to 7.5," arguing that they ignored the prefatory caveat to the statement they cite: "'*[i]n the absence of any evidence to the contrary*, we must presume that the use of . . . different terms in the claims connotes different meanings.'" *Id*. (citing *Applied Med. Res. Corp.*, 448 F.3d at 1333 n.3) (emphasis added by Takeda). According to Takeda, there is "evidence to the contrary" here, namely, the evidence from the specification and the common knowledge of those skilled in the art about the properties of enteric coatings, which support the conclusion that all three claim terms should be construed to state threshold pH levels, notwithstanding the different words used in these claim terms. *Id*. (citing *Baran v. Medical Device Techs., Inc*., 616 F.3d 1309, 1316 (Fed. Cir.2010) (any "implication [that different terms have different meanings] is overcome where . . . the evidence indicates that the patentee used the two terms interchangeably"). Takeda argues further that its proposed constructions *do* provide for different meanings for the different claim terms because each of the claim terms recites a different threshold level. *Id*. at 12.

Takeda also reiterates its position that the claim terms should be construed as being directed to dissolution "in the body," pointing to the evidence in the product literature and the specification linking pH ranges with the location in the gastrointestinal tract at which the enteric coating first dissolves. *Id*. at 12 (citing Charman Decl., Ex. 7[14] at DEX0014571; '755 patent, col. 6, l. 66 - col.7, l. 2 (describing the enteric coating of "composition (ii)" as a "usual enteric coat and layer which is dissolved at a pH of about 5.5" and "rapidly dissolved in the intestinal juice. . . .")). In addition,

[14]Although Takeda cites to Exhibit 8 rather than to Exhibit 7 in its brief, it is clear from the Bates number cited that this was a clerical error.

Takeda points to the prosecution history, arguing that the applicants stressed the release characteristics of the inventive compositions in the body when they stated: "By having composition (ii) dissolving at pH 5.0 - 6.0 . . . , the capsule formulation of claim 41 releases the active ingredient rapidly from composition (ii) at the pH of the small intestine." *Id*. (citing Cox Decl., Ex. 15 at DEX0006164 (emphasis added)). Takeda argues that "in the pharmaceutical field, pH-dependent enteric coatings commonly are understood to target release at a particular region of the body." *Id*. (citing Cox Decl., Ex. 16 (polymers identified in '755 patent); *id*., Ex. 14 (Reiland Dep.) at 66 - 67, 69 - 70, 71 - 72 (describing those polymers as dissolving in intestines); *id*., Ex. 17 (product insert for extended-release erythromycin product that Defendants' expert helped develop); *id*., Ex. 14 (Reiland Dep.) at 73:17 - 74:10 (describing that product as having a pH-dependent coating to optimize intestinal release)).

Takeda also rejects TWi's argument that these claim terms are indefinite. *Id*. at 12. First, Takeda points to the testimony of Dr. Reiland that he understood that the term "soluble" within a particular pH range referred to the property of a solid substance disappearing or dissolving into a liquid within the specified pH range, indicating that he did not find this term to be indefinite. *Id*. at 13 (Cox. Decl., Ex. 14 (Reiland Dep.) at 19:9 - 21:11). According to Takeda, the fact that Dr. Reiland disagrees with its proposed construction to the extent Takeda contends that the term refers to the *beginning* of dissolution in the body, is not sufficient to render these terms indefinite. *Id.* at 13 (citing *Haemonetics Corp. v. Baxter Healthcare Corp.*, 607 F.3d 776, 783 (Fed. Cir. 2010) ("A claim is not indefinite merely because parties disagree concerning its construction")).

Takeda also rejects TWi's assertion that the claim term that uses the word "layer" is indefinite because an enteric coating layer may contain insoluble material in addition to soluble polymers. *Id*. According to Takeda, Dr. Reiland "did not opine that the presence of even as much as 25% of insoluble excipients in a coating layer would affect the pH level at which the enteric polymer would dissolve;" in any event, it contends, even if other excipients might affect the pH at which the layer dissolved, one skilled in the art could determine that through testing. *Id*. (citing Cox Decl., Ex. 14 (Reiland Dep.) at 58 - 59, 108 - 110).

Addressing the claim term "released in the pH range of no less than 5.0 to no more than 6.0," Takeda rejects TWi's reliance on the following statement in the specification that TWi contends equates release of the active ingredient with dissolution of the enteric coating: "the coating material is dissolved/eluted under the circumstances of more than a certain pH value *to release an active ingredient*." *Id*. (citing '755 patent, col. 9, ll. 32 - 35 (emphasis added by Takeda)). Takeda argues that during prosecution, the applicants also used the "soluble" and "release" terms similarly. *Id*. In particular, Takeda points to the fact that even though the claim term relating to composition (i) refers to the polymeric substance as "s*oluble* in the pH range of 6.0 to 7.5," the applicants described both compositions (i) and (ii) in terms of *release* of active ingredient, stating as follows: "[c]omposition (i) releases the active ingredient at pH 6.0 - 7.5, and composition (ii) releases it at pH 5.0-6.0. The two-composition formulation . . . releases the active ingredient at two different pH . . . ." *Id*. (quoting Reiland Decl., Ex. I at DEX0006162). Takeda also cites to the following statement in the prosecution history to illustrate this point: "By having composition (ii) dissolving at pH 5.0-6.0, . . . the capsule formulation of claim 41 releases the active ingredient rapidly from composition (ii) at the pH of the small intestine." *Id*. (quoting Reiland Decl., Ex. I at DEX0006164). According to Takeda, "[r]ather than suggesting indefiniteness . . . these statements merely recognize that, where the enteric coating is the delayed-release mechanism, 'release' occurs when that coating dissolves." *Id* at 13-14.

Takeda also rejects TWi's argument that the release limitation is indefinite because the patent does not specify the conditions of in vitro tests by which release of the active ingredient can be measured. *Id*. at 14. Takeda argues that the testimony TWi cites from Dr. Charman's deposition regarding in vitro dissolution tests does not relate to the actual claim language but rather, to a passage in the specification describing preferred rates of release for composition (i). *Id.* (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 90; '755 patent, col. 10, ll. 13 - 17 ("The rate of elution of active ingredient from the active ingredient release-controlled tablet, granule or fine granule thus obtained is desirably 10% or less for 5 hours in a solution of pH 6.0, and 5% or less for one hour and 60% or more for 8 hours in a solution of pH 6.8")). This testimony, therefore, does not support TWi's position, Takeda contends, because the claims are not limited to such a specific release

profile. Similarly, Takeda argues that other testimony by Dr. Charman that TWi cites relates to a specific in vitro release test described in a literature reference rather than to the actual claims of the patent. *Id*. (citing Jorjani Decl., Ex. 2 (Charman Dep.) at 77)).

Takeda further asserts that TWi "offers no evidence of the criticality of testing methodology under Takeda's actual construction of the 'release' term, i.e., 'begins to be released from the tablet, granule, or fine granule into the body at pH values within the range from 5.0 to 6.0.'" *Id*. Instead, Takeda argues, TWi challenges the term under a construction that ties the meaning of the claim to in vitro release using dissolution testing – a construction that is not offered by any party. *Id*. (citing Reiland Decl., ¶ 20 (stating that claim term "clearly refers to dissolution testing")). According to Takeda, in concluding that the release limitation refers to in vitro pH levels on the basis that "testing for release in the body at a given pH is not something that can be or is typically done in the art, " Dr. Reiland confuses indefiniteness with infringement analysis. *Id*. (citing Reiland Decl. ¶ 34; *Spansion, Inc. v. Int'l Trade Comm'n*, 629 F.3d 1331, 1346 (Fed. Cir. 2010) ("The difficulty or complexity of the infringement analysis does not necessarily speak to whether a claim is definite or not"); *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1354 (Fed. Cir. 2005) ("indefiniteness does not depend on the difficulty experienced by a particular person in comparing . . . the claims with allegedly infringing products or acts"); *SmithKline Beecham Corp. v. Apotex Corp*., 403 F.3d 1331, 1340-41 (Fed. Cir. 2005)).

Even if the release limitation were construed to refer to in vitro release, Takeda argues, it would not be indefinite. *Id.* at 15. Takeda notes that during prosecution, the applicants in fact submitted dissolution data to the Patent Office in which they contrasted the in vitro dissolution characteristics of the inventive composition to those of a prior art composition. *Id*. (citing Reiland Decl., Ex. 1 at DEX0007123-24). According to Takeda, the data was obtained using a test similar to the standard "buffer stage" test provided in the United States Pharmacopeia for delayed-release products, in which the applicants placed the two compositions in a buffer medium of pH 6.8 and tracked release over time. *Id*. Takeda argues that because the results reflected that the active ingredient from the inventive composition was fully released within 6 hours, in contrast to the prior art composition, a person of ordinary skill in the art would have known how to replicate tests set

forth in the patent specification to determine if a product met the in vitro profile of the inventive composition. *Id*. (citing Cox Decl., Ex. 14 (Reiland Dep.) at 135 -136 (testifying that a person skilled in the art would be familiar with, and could perform, the delayed-release dissolution tests included in the United States Pharmacopeia)).

Finally, Takeda argues that the facts here are distinguishable from those in *Honeywell Int'l., Inc. v. Int'l Trade Comm'n*, 341 F.3d 1340 (Fed. Cir. 2003), cited by TWi. *Id*.

2. Analysis

a. Whether the Claim Terms Are Indefinite

i. "active ingredient is released in the pH range of no less than 5.0 to no more than 6.0"

As noted above, "[b]ecause a claim is presumed valid, a claim is indefinite only if the claim is insolubly ambiguous, and no narrowing construction can properly be adopted." *Honeywell*, 341 F.3d at 1338 (citations omitted). TWi contends that the release limitation meets this standard for two reasons: 1) because a person skilled in the art would not know what methodology to use to determine whether this claim limitation is met; and 2) to the extent the word "release" is construed to mean "begins to release," a person skilled in the art would not know how much of the layer would have to dissolve to meet this limitation. The Court rejects both arguments.

First, the Court concludes that because this claim limitation does not specify a particular method for testing whether the range stated in it is met, the question of what testing methodology should be used is one of infringement and not indefiniteness. The Court's conclusion is based on the well-established rule that "[t]he test for indefiniteness does not depend on a potential infringer's ability to ascertain the nature of its own accused product to determine infringement, but instead on whether the claim delineates to a skilled artisan the bounds of the invention." *SmithKline Beecham Corp. v. Apotex Corp*., 403 F.3d 1331, 1340-41 (Fed. Cir. 2005). In *SmithKline*, the asserted claim "recited in clear terms a discernible chemical structure" for the claimed compound but the district court limited the claim to "commercially significant amounts" of the compound on the basis that if the term were construed more broadly to include "any amount, however small or insignificant," potential infringers would not be able to determine whether their products infringed the claim and

the claim would be indefinite. *Id*. at 1335. The Federal Circuit rejected the district court's reasoning, stating as follows:

> In this case, the problem for Apotex is that it cannot accurately ascertain the nature of its own product. The scope of this claim is clear; the infringement of the Apotex product is not. Even if a claim is broad enough to embrace undetectable trace amounts of the claimed invention, "[b]readth is not indefiniteness." *In re Gardner*, 57 C.C.P.A. 1207, 427 F.2d 786, 788 (CCPA 1970).

Id. at 1341.

In *SmithKline*, the Federal Circuit distinguished *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464 (Fed. Cir.1993), which was cited by the defendant for the proposition that a claim is indefinite if it is "'not sufficiently precise to permit a potential competitor to determine whether or not he is infringing.'" *Id.* at 1340 (quoting *Morton*, 5 F.3d at 1470). The court explained:

> The *Morton* case . . .does not hold that the inability to detect the claimed compound in the infringing device renders a compound claim indefinite. Rather, *Morton* stands for the unremarkable proposition that a compound claim, to be definite, must apprise a skilled artisan of the bounds of the claim. The record in *Morton* contained "considerable evidence showing that those skilled in the art could not make the claimed compounds using the procedures of the specification, and no evidence that such compounds even exist."

Id. (quoting *Morton*, 5 F.3d at 1469-70). Here, as in *SmithKline*, the claim term at issue is clear, even if the parties may disagree on the question of what testing should be conducted to determine whether Defendants are infringing.

Honeywell Int'l, Inc. v. Int'l Trade Comm'n does not stand for a contrary result. In that case, the claims were directed to a method of manufacturing spun yarn which, at certain steps of the method, required the yarn to have a "melting point elevation" temperature ("MPE") within a specified range. 341 F.3d at 1339. At the time of the invention, there were at least four different methods of measuring the MPE, each of which could yield a different MPE value. *Id*. Three possible constructions were proposed – an "any one method" construction (under which the claim would be satisfied if the MPE was within the specified range using any of the four methods), an "all methods" construction (under which the claim would be satisfied only if the MPE was found to be within the specified range using *all* of the tests) and the "ball method" construction (under which the claim would be satisfied only if the MPE was within the range specified when measured using a method called the "ball method" that was argued to be the most appropriate one in light of the patent

claims and specification). *Id*. The court concluded that none of these constructions was appropriate because "the claims, the written description, and the prosecution history failed to give [the court], as the interpreter of the claim term, any guidance as to what one of ordinary skill in the art would interpret the claim to require." *Id*. at 1340. The court further noted that although there was extrinsic evidence derived from proprietary documents of the plaintiff showing that the "ball method" was more practical than the others, it would be improper to import limitations from these publications to the extent that they were outside the bounds of the intrinsic evidence and even of any written publication. *Id*. at 1341. Because the sample preparation method was critical to practicing the invention, the court in *Honeywell* concluded that a skilled artisan would not know the bounds of the claim, rendering it indefinite. *Id*.

The Court finds the facts here to be distinguishable from those in *Honeywell* because in that case, different yarns would be created depending on which sample preparation method was used. *Id*. As a result, without guidance as to which method should be used, a skilled artisan would be unable to read the claim and make the claimed invention. This case does not involve a production process and the testing method is *not* critical to the claim limitation. Therefore, the holding in *Honeywell* is not applicable here. *See Alza Corp. v. Mylan Laboratories, Inc.*, 349 F. Supp. 2d 1014 (N.D.W.Va. 2004) (distinguishing *Honeywell* and holding that claim for sustained release drug was not indefinite even though it set forth ranges of time in which drug released because method for testing was not crucial part of the claim).

Second, the Court rejects TWi's assertion that the term is indefinite because the intrinsic evidence does not offer guidance as to the percentage release necessary to meet the "begins to release" requirement. The Court notes that the phrase "begins to release" is not a claim term but merely a proposed construction intended to convey the idea that the pH values in the term represent a threshold. Further, while TWi has cited deposition testimony by Takeda's expert stating that it would be impossible to state the percentage that would constitute what "begins to release" means, it has not cited to any expert testimony suggesting that this concept would have been insolubly ambiguous to a person skilled in the art. Therefore, the Court rejects this argument.

ii. "said polymeric substance is soluble in the pH range of 6.0 to 7.5" and "a layer soluble in the pH range of no less than 6.5 to no more than 7.0"

TWi argues that these claim terms are indefinite for the same reasons the release limitation is indefinite and for the additional reasons that: 1) the inventors use the word "soluble" in these claim terms in a manner that is not consistent with its common usage in the art, using it to mean "some form of release;" and 2) the word "layer" renders these terms ambiguous. As to the indefiniteness arguments that duplicate the ones asserted in connection with the release limitation, the Court rejects those arguments for the reasons stated above. The Court also rejects TWi's arguments based on the word "soluble" and "layer."

TWi's expert opines that the inventors used the term "soluble" in the '755 patent in a manner that is inconsistent with its generally accepted meaning in the art, namely, to refer to "when the active ingredient is released." Reiland Decl. ¶ 47. Takeda does not disagree. *See* Reply Claim Construction Brief at 13. To the contrary, Takeda notes that in the claims and specification, as well as during the prosecution history, the words "soluble" and "release" were used similarly to reflect the idea that where the enteric coating is the delayed-release mechanism, "release occurs when the coating dissolves." As patentees can create their own lexicon, the mere fact that the word "soluble" is used in a manner that differs from its ordinary and customary meaning in the '755 patent does not render these claims indefinite. Thus, TWi's argument boils down to whether the claims are indefinite because a person skilled in the art would not know what testing methodology to use to determine the point at which the layer becomes soluble, that is to say, when the active ingredient is released. For the reasons discussed above, the Court concludes that this argument fails because the claims do not require that any particular test be used.

The Court also finds unpersuasive TWi's contention that the use of the word "layer" in these claim terms renders them indefinite because the layer could contain excipient materials that are not soluble. Although Dr. Reiland stated in his declaration that insoluble excipients are often used in coatings and that these never dissolve or become soluble, *see* Reiland Decl. ¶ 51, he does *not* state that the coating would not dissolve sufficiently to release the active ingredient because of these excipients. Further, when asked at his deposition whether a coating that included up to 25% non-

soluble excipients would dissolve sufficiently to release the active ingredient, Dr. Reiland testified that he could not say. *See* Cox Decl., Ex. 14 (Reiland Dep.) at 108-110. Therefore, the Court rejects TWi's assertion that the word "layer" renders this claim term indefinite.

b. Whether Claim Terms Should be Construed Based on Plain Language or Rather as Stating Threshold Values

Handa and Impax argue that these claim terms should be construed according to their plain meaning, rejecting Takeda's assertion that the values represent threshold values at which release begins. Because this position flies in the face of the intrinsic evidence and the knowledge of a person of ordinary skill in the art, the Court rejects Handa and Impax's position and instead finds that Takeda's proposed constructions are correct to the extent that they make clear that the ranges represent threshold values.

First, the '755 claims themselves support Takeda's position. In particular, claim 1 includes a list of polymers suitable for the "layer soluble in the pH range of no less than 6.5 to no more than 7.0." As Defendants' expert, Dr. Reiland, conceded, although all of these polymers begin to dissolve at threshold pH levels of between 6.5 and 7.0, all of them also are soluble at pHs above 7. *See* Reiland Dep. at 28 - 29, 31 - 32, 112 - 118. Thus, claim 1 would make no sense if Defendants' position were adopted. *See Talbert Fuel Sys. Patents Co. v. Unocal Corp.*, 275 F.3d 1371, 1376 (Fed. Cir. 2002), vacated and remanded on other grounds, 537 U.S. 802 (2002).

Second, the specification supports Takeda's position because it makes clear that enteric coatings dissolve and release drug at and above particular pH levels. *See* '755 patent, col. 9, ll. 32 - 35 ("'pH-dependently' means that the coating material is dissolved/eluted under the circumstances of more than a certain pH value . . . "). Similarly, the prosecution history reflects the understanding that the claimed ranges referred to threshold values. *See* Reiland Decl., Ex. I at DEX0007130 (noting that "composition (ii), which is soluble at lower pH than 6.8 such as pH 5.0-6.0 . . . releases the active ingredient rapidly at pH 6.8").

Third, the marketing materials describing the products referenced in the specification also support the conclusion that a person skilled in the art would understand that these claim terms recited threshold values. For example, the literature describing the Eudragit and Shin-Etsu polymers

describes these coatings with reference to the pHs above which each dissolves. *See* Charman Decl., Exs. 6-8. Indeed, the evidence presented by Takeda, which appears to be undisputed, reflects that *none* of the exemplary polymers listed in the specification is soluble only in the pH range of pH 5.0 to 6.0, or in the pH range of pH 6.5 to 7.0. *Id.*

Finally, the Court is not persuaded by Defendants' contention that the claim terms that use "no more/no less" must have a different meaning than the term that does not. The overwhelming intrinsic and extrinsic evidence supports the conclusion that all of these terms recite threshold value ranges. Therefore, the presumption that different words carry different meanings is rebutted.

c. Whether the Court Should Include "in the body" and "in the gastrointestinal tract" in its Construction

The parties dispute whether these claim terms should be construed to include the words "in the body" or "in the gastrointestinal tract." Defendants rely on the references in the specification to McIlvaine or Clark-Lubs solutions, whereas Takeda cites to evidence that these solutions were merely used as surrogates for the pH in the gastrointestinal tract. While the Court agrees with Takeda that the invention is directed to release of active ingredient at certain points in the body, or gastrointestinal tract, it is not clear why these limitations should be included in the construction of these claim terms, given that these ranges could be met using these "surrogate" solutions outside the body. Therefore, the Court declines to include these proposed limitations in its claim construction.

V. CONCLUSION

For the reasons stated above, the Court adopts the following constructions:

"a crystal of" ('058 patent, claims 1-4/ '668 patent, claims 9-10), "a crystalline compound of" ('276 patent, claims 2 and 3/ '971 patent, claims 6-8)	regularly repeating pattern of molecules with long range order extending in three dimensions
"characteristic peaks at interplanar spacings (d)" ('058 patent, claims 1 and 2/ '971 patent, claims 7 and 8)	peaks in the X-ray powder diffractogram of a crystal that uniquely identify that crystal, denoted by distances between lattice planes in a crystal as measured by a diffraction experiment and defined by Bragg's law, within normal experimental error of X-ray powder diffraction.

"effective amount" ('971 patent, claim 5)	an amount sufficient to help ameliorate or cure reflux esophagitis
"about" ('668 patent, claims 9 and 10)	approximately
"amorphous compound" ('282 patent, claims 1 and 2)	a non-crystalline solid that lacks the long-range order characteristic of a crystal
"released in the pH range of no less than 5.0 to no more than 6.0"	begins to be released from the tablet, granule, or fine granule at pH values within the range from 5.0 to 6.0
"soluble in the pH range of 6.0 to 7.5"	begins to dissolve at pH values within the range from 6.0 to 7.5
"soluble in the pH range of no less than 6.5 to no more than 7.0"	begins to dissolve in the gastrointestinal tract at pH values within the range from 6.0 to 7.5

IT IS SO ORDERED.

Dated: April 11, 2012

JOSEPH C. SPERO
United States Magistrate Judge